

University of Dundee

## MASTER OF SCIENCE

### Analysis of outcomes following emergency admission in patients with dementia and/or cognitive impairment and/or delirium

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# **Analysis of Outcomes Following Emergency Admission in Patients with Dementia and/or Cognitive Impairment and/or Delirium**

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**Submitted for the degree of Master of Science by Research in Medicine**

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## **Declaration of the MSc Student**

I declare that I am the author of this thesis; that the work of which this thesis is a record has been done by me, and it has not previously been accepted for a higher degree. I also state that all references cited has been consulted by me personally and the conditions of the relevant ordinance and regulations have been fulfilled.

Dundee,

23-09-2015

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# Abstract

## Background

In general hospital settings, acute admission patients with confusion, whether due to dementia, delirium or other cause often get a worse outcome compared with other patients. In addition, unidentified dementia or cognitive impairment is frequent in general hospital, which contributes to some healthcare outcomes such as length of stay, mortality and re-admission for the dementia population.

A systematic review on prevalence, associations and outcomes of dementia in older people admitted to general hospital, which has been the only review that covers a comprehensive comparison of heterogeneous studies so far.

## Methods

Systematic searches were conducted using MEDLINE, EMBASE, PsycInfo, CINAHL and the Cochrane library. All types of studies were included in the reviews. Only those studies published in English and targeted in people aged 65 years and above were involved. Meta-analysis was performed with Cochrane's Review Manager5.3. Heterogeneity of included studies would be measured by  $I^2$  which can explain the percentage of the variability in effect due to heterogeneity.

The data come from a routine clinical identification programme called Cognitive Geriatric Assessment research (CGA), which was a retrospective cohort study conducted with patients aged above 65 years' old who have an admission to acute hospital. Patients with admission between 01 January 2012 and 31 December 2012 were all involved in the study. The data analyse were conducted using SAS version9.3 provided by the server of the Safe Haven of Health Informatics Centre (HIC) in Dundee University. Characteristic differences across the people were checked for significance using  $\chi^2$  tests and ANOVA tests. Kaplan-Meier procedures and Log-Rank Tests were conducted to describe the median survival time and survival difference. Cox's proportional hazards regression model was employed to investigate the association between death and survival time with multiple predictors.

To check the validity of the survival model, Kolmogorov-Type Supremum Tests (49) with the 'assess' statements in SAS were also added in the final model.

## Results

There were total of 14 papers included in the systematic review. Meta-analysis of 6 papers with 30 days' mortality showed that people with dementia had significantly greater mortality by 11% (95%CI: 6%-16%,  $p < 0.001$ ) compared with people without dementia, though with significant heterogeneity ( $I^2 = 68\%$ ,  $p = 0.01$ ). The longest stay was 26.1 days; the minimum length was 4.6 days.

In unadjusted Cox's model, the hazard of death was associated with dementia, clinical delirium, FSD and CI as well as some demographic factors. When adjusting for the four conditions, age, gender CCI and SIMD, the hazard of death for patients with dementia was estimated to decrease slightly from 1.42 unadjusted to 1.17 with a 95% confidence interval of 1.00 -1.38 . Similarly, those with clinical delirium had 1.23 times greater hazard ratio (HR) to death (95% CI: 1.10-1.37) which also declined from 1.39 when no factors were adjusted for. Although FSD and CI were shown to significantly increase the risk of death with hazard ratios of 1.53 and 1.35 by themselves, they were not significant predictors anymore in the adjusted model. Age, male gender and CCI always significantly contributed to predicting the hazard of death no matter what was adjusted for.

## Conclusion

During admissions for the elderly, the four confusion conditions are prevalent worldwide. Each confusion condition is related to worse outcomes in general hospital settings. People with dementia, delirium, cognitive impairment and FSD always do badly in terms of survival time. Dementia and delirium indeed have independent significant influence on mortality when other factors are taken account of in an adjusted Cox regression model. It is crucial to identify CI in a timely way, which potentially could decrease mortality. For patients who have already been diagnosed with some chronic diseases, it will also benefit them if their CI can be detected early and possible treatment earlier.

### **Keywords**

Dementia; Cognitive Impairment; Clinical Delirium; Systematic Review; General Hospital; Survival Analysis.

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## Abbreviations

A-CGA = Acute Comprehensive Geriatric Assessment;

ADL = Activities of Daily Living;

AMT = Abbreviated Mental Test;

APACHE II = Acute Physiology and Chronic Health Evaluation II;

CAM = Confusion Assessment Method;

CCI = Charlson Comorbidity Index;

CGA = Comprehensive Geriatric Assessment;

CHI = Community Health Index;

CI = Cognitive Impairment;

95%CI = 95% Confidence Intervals;

CINAHL = Cumulative Index to Nursing and Allied Health;

CIRS-G = Cumulative Illness Rating Scale-Geriatric;

CVD = Circulatory System Disease;

DEMQOL= Dementia Quality of Life measure;

DRS = Delirium Rating Scale;

DSM = Diagnostic and Statistical Manual of Mental Disorders;

EMBASE = ExcerptaMedica database;

FSD = Fully Syndromic Delirium;

GDS = Geriatric Depression Scale;

GHQ = General Health Questionnaire;

GRO = General Registrar Office;

HIC = Health Informatics Centre;

HR = Hazard Ratio;

ICD = International statistical classification of disease;

IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly;

MEDLINE = Medical Literature Analysis and Retrieval System Online;

MeSH = Medical Subject Headings;

MMSE = Mini-mental State Examination;

OPRAA= Older Persons Acute Assessment

SD = standard deviation;

SIDAM = Kurz-Skala Stimmung/Aktivierung;

SIMD = Scottish Index of Multiple Deprivation score;

SMR = Scottish Morbidity Records;

TASC = Tayside Academic Science Collaboration;

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# 1. Introduction

## 1.1 Background

As a disease associated with old age, dementia has become a concern not only to the older people but also to the majority of the general citizens. The worldwide prevalence of dementia among the elderly is rapidly growing. It is estimated that about 35 million people living with dementia globally in 2010, and this figure is projected to grow further at two times in every year. Elderly people with cognition impairment suffered from disability, low life expectancy and low quality of life. Sometimes, they are even misunderstood by their friends. Caring for relatives or patients with dementia or delirium is also a huge task. Besides, the medical costs for formal and social care for these groups of people are huge.

People with ages always suffered problems with memory and cognitive abilities, which are often considered as normal for the age. Unfortunately, the early stage of dementia is usually marked by increasing deterioration in cognition. Some cognitive impairment does not reach the severity of dementia. The slow onset of confusion may cause the neglect on diagnosis of dementia. Delirium is an urgent symptom, which may cause by varied cause such as adverse effects, infection and intra-cranial. Patients are often misdiagnosed as dementia rather than having a medical problem. The similar confusion symptom and course of disease may them easily overlap and mix together.

According to official statistics, there are 850,000 people living with dementia in the UK now and this figure is estimated to rise to over two million by 2051 if no action has been taken(1). In general hospital settings, acute admission patients with confusion, whether due to dementia, delirium or other cause often have a worse outcome compared with other patients. For example, dementia patients are shown to do badly in survival time in many studies (2, 3). The mortality from dementia is estimated to be 4 times that of no-dementia(4). Unidentified dementia, delirium or cognitive impairment is frequent in general hospital, which contributes to some

healthcare outcomes such as length of stay, mortality and re-admission for the dementia population. In one study, the 6-month mortality for patients with undetected delirium was three times than patients for whom delirium was identified(5). Besides, the reality that “dementia” is always thought as a common co-morbidity in acute hospital admission but is rarely recorded as a primary reason for admission also means there is a lack of data in these studies.

A systematic review has been done before to examine the range of diagnostic tools used in general hospital settings, also the prevalence and associations of dementia under general hospital settings. Finally, fourteen papers were identified. The prevalence of dementia was ranged largely. Less than 30% of studies screened for delirium or depression, which may cause misclassification for having dementia. This review was valuable for us to highlight the gaps in the literature and assess the method used in the work which has published. But some limitations such as less rigorous searching procedure and outdated papers involved all raise up to conduct a further review.

## **1.2 Aims and Objective**

Our aim was systematically review the prevalence and outcomes of elderly who have confusion conditions who admitted to the general hospital. Also try to clarify the effect of each confusion condition on patients’ outcomes by analysing a dataset.

## **1.3 Systematic Review**

### **1.3.1 Previous Study**

A systematic review about prevalence, associations and outcome of dementia in older people admitted to general hospital, published in 2011 by Mukadam(6), was found to be relevant to my study. This is the only review that covers a comprehensive comparison of heterogenous studies. But in this paper there are several weaknesses that cannot be ignored. Firstly, they just used two keywords “cognitive impairment” and “dementia” as the terms in the searching stage, which was too focused and ignored outcomes. Second, dementia is a common condition that



affects about 800,000 people in the UK(7) and the risk of developing dementia will increase as you get older, and the condition usually occurs in people over the age of 65. Several studies have explored prevalence of dementia before. In total, there were over 30% of people over 65 who will develop dementia (8-10). However, the age cut-off point which was used by Mukadam(6) was 55 years. For geriatric conditions, such an age boundary is too young to get a satisfactory search result. Third, the paper only included the studies which used validated diagnosis criteria for dementia. It excluded the dementia population without a formal diagnosis. Furthermore, we can find that among 14 papers presented in Mukadam's(6) review, six of them were published before 1994. It is therefore essential to do a more thorough review to find studies conducted with dementia for the more recent 20 years.

The proposed study will use several alternative MeSH terms within the search, which might be expected to include important articles. Also by including patients with all forms of cognitive impairment regardless of whether they have a formal diagnosis of dementia can be representative of the whole dementia population rather than those solely with a formal diagnosis.

### **1.3.2 Methods**

The review was carried out as a follow-up to a study on Cognitive Geriatric Assessment (CGA) on patients in Fife, Scotland which was conducted from 2011. All people aged 65 years and over admitted as an emergency to NHS Fife have been assessed for functional and cognitive ability, screened for delirium, and had their socio-environmental situation documented.

#### **Search strategy and selection criteria**

Systematic searches were conducted using electronic databases from 1994 to October 2014, including MEDLINE (Medical Literature Analysis and Retrieval System Online), EMBASE (Excerpta Medica data BASE), PsycInfo, CINAHL EBSCO (Cumulative Index to Nursing and Allied Health) and the Cochrane library. The following MeSH terms were combined and used:

(“Dementia” or “Alzheimer Disease” or “mild cognitive impairment” or “cognitive impairment” or “cognition disorder”)

AND

("Hospitals, general" or "hospitals" or "hospital units" or "emergency services, hospital" or emergency treatment" or "emergency medical services" or "patient admission" or "hospitalisation")

AND

("Patient outcome assessment" or "outcome assessment (health care)" or "patient readmission" or "patient discharge" or "patient transfer" or "comorbidity")

All types of studies (for example, cohort and cross-sectional studies) were included in our reviews. Only those studies published in English and targeted in people aged 65 years and above were included.

#### **Inclusion criteria**

- Studies focused on people aged 65 years and above (if the paper explore more widen age range, we would also keep the paper, but just extracted outcome of people aged 65 and above).
- Studies were published in English.
- Studies were published from 1994 onwards.
- Studies conducted in general hospital. Emergency wards within the general hospital were also included.

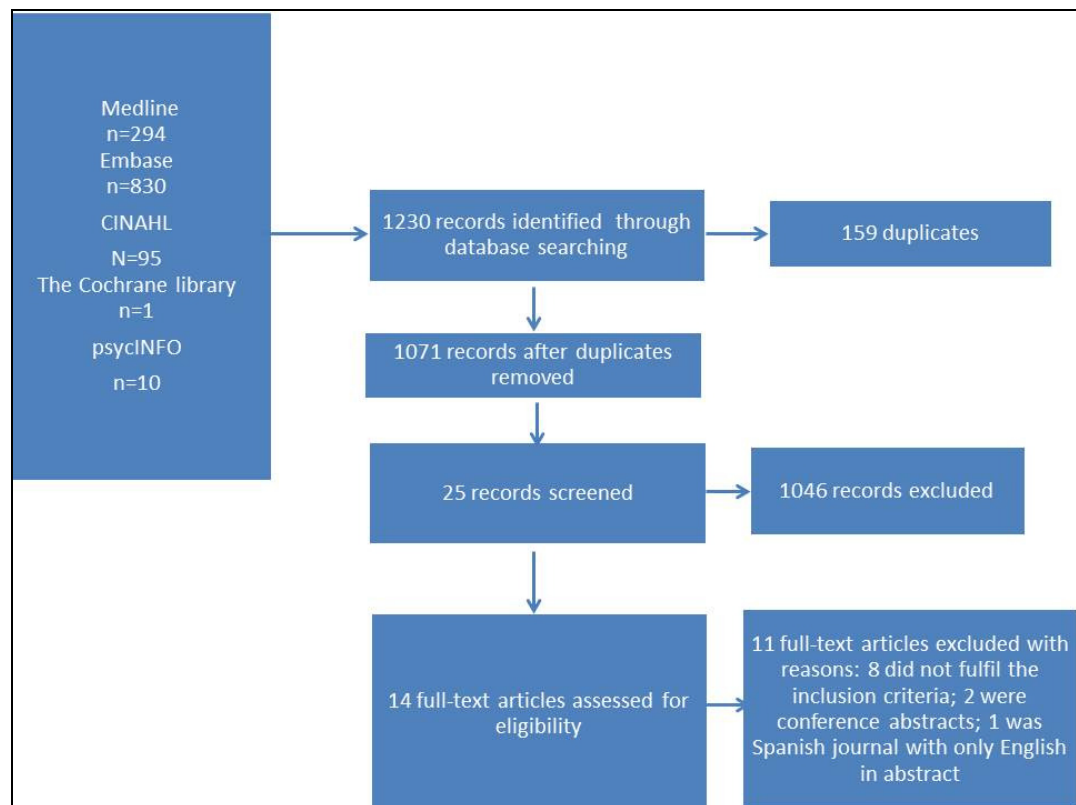
#### **Exclusion criteria**

For the patients with hip fracture, cognitive impairment (including dementia and delirium) rate is believed to be as much as three to six times higher than other general hospitalized older patients(11), so the studies involving hip fracture and any surgical emergencies were excluded.

#### **Study selection**

All the search results will be exported into EndNote X6 from each database. The results will first be selected by deleting the duplicates by EndNotesystematically. And then a selection based on title and abstract will be done. In case of uncertainty

for inclusion, titles and abstracts will be assessed for inclusion by two reviewers. Discrepancies in inclusion will be resolved by discussion with Professor Peter Donnan (P.D.). Next, those studies still remaining based on title and abstract will be accessed in full text and be appraised further.



*Figure 1.1 Study flowchart*

### 1.3.3 Data Extraction and Quality Assessment

#### Data extraction

Detailed information about each study was extracted with disagreements resolved by consensus with P.D. Several data extraction forms (Table 1.1 to Table 1.4) were designed to collect information on characteristics of each study. Variables of the forms include setting and type of study, age range of the samples, sample size, the assessment tools used, prevalence of dementia/delirium/cognitive impairment, length of hospital stay, mortality and rehospitalisation rate.

## Quality assessment

Selected studies for methodological quality were appraised by using the assessment tool STROBE Statement(12). The STROBE Statement has been instituted for addressing three main study designs of analytical epidemiology: cohort, case-control and cross-sectional studies. A checklist of 22 items was presented in order to improve the reporting quality of observational studies. The study design, details on recruitment of participants, study size, randomization, quantitative variables, main outcome, harms and especially potential funding all would be checked with the STROBE for quality assessment.

### 1.3.4 Data Analysis

Meta-analysis was performed with Cochrane's Review Manager 5.3(13) Mean Differences (MD) with 95% confidence intervals (CIs) of mortality were used to estimate differences between people with dementia and people without dementia. Pooled mortality rate and 95% CIs were determined by using random effects model. I calculated 95% CI to estimate the variability around the mean mortality of each study group. The formula as following:

$$Proportion \pm 1.96 \times \sqrt{\frac{Proportion \times (1 - Proportion)}{Sample Size}}$$

Heterogeneity of included studies would be measured by  $I^2$  which can explain the percentage of the variability in effect due to heterogeneity.

### 1.3.5 Results

#### Study selection

Flowchart of the selection process can be seen in Figure 1.1. Initially, a total of 1230 potential references were identified with the search strategy (294 through Medline, 830 through Embase, 95 through CINAHL, 1 through the Cochrane library and 10 through psycINFO)(Figure 1.1). Among the 1230 publications, 159 were duplicates(12.9%). 1046 articles were excluded based on the information provided by the titles and abstract mainly because some of them were found to be not related to my research. After that, there were 25 full text articles screened. Among these articles, Sampson et al has published separately two articles in 2009 and 2013 with

almost the same study. I decided to include all of them and numbered them as ① a. and ① b. as they were believed not identical. Finally, 11 articles were excluded as 8 of them did not fulfil the inclusion criteria, 2 of them were conference abstracts and 1 of them was a Spanish journal with only English in the abstract.

### **STROBE statement quality**

The result of applying the STROBE statement has been shown in Appendix 1. We can see that almost every article has done well in title, abstract, introduction and discussion sections. Some of the items were not applicable such as 6B '*Matching for Participants*', 12D '*Sensitivity Analyses*', 16C '*Translating for the Main Result*' or 17 '*Report Other Analyses Done*'. Generally, we believed that these articles were reasonable quality although some were not applicable such as '*Definition of Exposure*', '*Potential Confounders*' and '*Effect Modifiers*'.

### **Settings, methodology and characteristics of papers**

The final 14 articles' information is presented in Table 1.1. Except for one paper that did not specify the study setting, the other 13 papers were all conducted within general hospitals. Among these 14 papers, 9 were prospective cohort study, 3 were retrospective cohort study, and 2 were case control study and randomised control study respectively. Sample sizes differed greatly from each study. For retrospective cohort studies, the sample size would reach up to 3354017. However, for prospective cohort studies, sample size ranged from 250 to 794. Patients of studies also based on a numbers of countries (6 from UK, 2 from USA, one each from Spain, Germany, Australia, Netherland, Switzerland and China). In total, there were 8 papers mentioned screening for delirium. Most common screening tools for it were Confusion Assessment Method (CAM) (8), as 4 papers have used this method. 10 papers have described dementia diagnosis, 4 of them used Diagnostic and Statistical Manual of Mental Disorders (DSM) (14). Besides, among 10 papers which had the cognition screen, the most prevalent method for diagnosis was Mini-mental State Examination (MMSE) (15).

Table 1.1 Characteristic of 14 inclusion articles

Paper	Setting	Type of study	Exclusion criteria	Age range (mean, SD)	Female %	Sample size	Delirium screen	Dementia screen	Cognition screen	Other assessment tools
①a Sampson et al.(16)(2009) UK, British Journal of Psychiatry	Medical acute admissions unit	Prospective cohort study	Admitted<48h, did not speak sufficient English, admitted to surgical specialties, gynaecology, ear nose throat ophthalmology, cognitive impairment caused by delirium, delirium, discharged before assessment, refused consent	>70 (83, no SD given)	59	617	CAM	DSM-IV	MMSE	Functional Assessment, Staging (FAST) Scale, Waterlow Scale, Charlson Co-Morbidity Scale, APACHE II, ICD-10
①b Sampson et al.(17)(2013) UK, International Journal of Geriatric Psychiatry	General Hospital	Prospective cohort study	Admitted<48h, did not speak sufficient English	>70 (83, no SD given)	59	616	CAM	DSM-IV	MMSE	Waterlow Scale, ICD-10, Charlson comorbidity scale, APACHE II, Functional Assessment Staging Scale
②Guíjarro et al.(18)(2010) Spain, Neuroepid	General hospitals	Retrospective cohort study	None	>65	NA	3354071	NO	ICD-9-CM	NO	NO

Paper	Setting	Type of study	Exclusion criteria	Age range (mean, SD)	Female %	Sample size	Delirium screen	Dementia screen	Cognition screen	Other assessment tools
<b>emiology</b> <b>③ Whittamore et al.(19) (2014) UK, International Journal Of Geriatric Psychiatry</b>	Acute geriatric medical ward, trauma orthopaedic ward, general medical ward	Prospective cohort study	Discharged prior to reasons approached, repeatedly unavailable, too ill to screen, already in a study, refuse screen, no English	≥70 (84, no SD given)	66	250	DRS-R-98, DSM-IV	Not specified	MMSE	Neuropsychiatric Inventory, Cornell Scale for Depression in Dementia, Modified Early Warning Score, Charlson Scale, Frailty index, Barthel Index
<b>④ Kennedy et al.(20) (2014) UK, Journal of the American Geriatrics Society</b>	Urban tertiary care ED	Prospective observation cohort study	Non-English speaking, inability to provide informed consent, non-availability of a surrogate for informed consent, high acuity of illness	≥65 (77, no SD given)	51	700	CAM	NO	MMSE, Delirium Symptom Interview, Memorial Delirium Assessment Scale, Attention test,	APACHE II score
<b>⑤ Eeles et al.(21) (2010) UK, Age and Ageing</b>	General medical service	Prospective cohort study	Unavailability of proxy consent	≥75 (82.5, 5.6)	NA	278	DSM-IV	NO	IQCODE-10, MMSE	Greenfield Index, Charlson morbidity score, Barthel Index score

Paper	Setting	Type of study	Exclusion criteria	Age range (mean, SD)	Female %	Sample size	Delirium screen	Dementia screen	Cognition screen	Other assessment tools
⑥Bickel et al.(22) (2006) Germany, Dementia and Geriatric Cognitive Disorders	General hospital	Prospective cohort study	Very severe physical illness, complications were to be expected due to participation in the study, previously extant dementia, residence in a nursing home, the need for nursing care, blindness or deafness, inadequate facility in German, imminent release within 48 h	Age between 65 and 85 (75.2, 5.5)	59.1	79 4	NO	DSM-III-R, DSM-IV, ICD-10	SIDAM	Cambridge Examination for Mental Disorders of the Elderly, KUSTA, Comorbidity Index
⑦Draper,B et al. (23) (2011) Australia, International Psychogeriatric	Admitted patient care database	Retrospective cohort study	NA	>50 *	NA	25 30 00	ICD-10-AM	ICD-10-AM	NO	
⑧ Buurman, B et al. (24)(2011) Netherland , PLoSONE	General internal medicine wards	Prospective multicentre cohort study	Did not provide informed consent, unable to speak or understand Dutch, came from another ward inside or outside	65 (78.2,7.8 )	53.8	63 9	CAM	NO	MMSE	CGA, The Charlson co-morbidity Index, ICD-9, IQCODE-SF



Paper	Setting	Type of study	Exclusion criteria	Age range (mean, SD)	Female %	Sample size	Delirium screen	Dementia screen	Cognition screen	Other assessment tools
			the hospital, transfer to the ICU, the Coronary Care Unit or another ward in or outside the hospital within 48 hours of admission, terminally ill							
⑨ Goldberg, S E et al.(25)(2013) UK, BMJ(Online )	Acute medical admission unit	Randomised control trial	Patients with a clinical need for another specialist service	>65 (85, no SD given)	52	600	DRS	NO	MMSE	DEMQOL, EuroQoLED-5D, short London handicap Scale, neuropsychiatric inventory, Barthel index, carer strain index, general health questionnaire, GHQ-12, carer's satisfaction, Likert Scales
⑩ Dodson, J.A . et al. (26)(2013) USA,	Not specified	Prospective cohort study	Non-English speaking, admitted from a nursing home, had isolated right-side heart failure, were	65 (80,8)	53.2	282	NO	NO	MMSE	NO

Paper	Setting	Type of study	Exclusion criteria	Age range (mean, SD)	Female %	Sample size	Delirium screen	Dementia screen	Cognition screen	Other assessment tools
<b>American Journal of Medicine</b>			found to be delirious on the basis of the Confusion Assessment Method, being dependent in ≥3 activities of daily living 2 weeks before admission							
<b>⑪ Joray,MD et al.(27) (2004) Switzerland, The American Journal of Geriatric Psychiatry</b>	General internal-medicine service	Prospective cohort study	Discharge within 24 hours, previously living in a nursing home, transfer from another hospital for an elective procedure, had private insurance, unstable medical conditions, aphasia or stroke, terminal illness or coma, inability to give a correct name and date of birth	≥75 (82.4,5.0 )	60.9	40 1	NO	NO	MMSE	ADL Scale, Lawton Instrumental ADL scale, GDS
<b>⑫ Li Fang et al.(28) (2013) China, Aging AND Experiment</b>	Department of Neurology	Retrospective case-control study	Brain dysfunction due to psychiatric disease, drug abuse, severe neurologic impairment that affected completion of the	≥60(75.8 2,7.42)(dementia)	37.15( dementia)	34 88 8	NO	DSM-IV-TR, Statistical Manual of Mental Disorders, MMSE, NINCDS-	NO	ICD-10, CIRS-G

Paper	Setting	Type of study	Exclusion criteria	Age range (mean, SD)	Female %	Sample size	Delirium screen	Dementia screen	Cognition screen	Other assessment tools
<b>al Research</b>			psychological evaluation or physical examination					ADRD, NINDS-Airen, Hachinski Ischemic Scores		
<b>⑬ Daiello, L.A et al. (29)(2014), USA, Archives and Gerontology and Geriatrics</b>	Fee-for-services Medicare administrative claims data	Retrospective cohort study	Less than 30 days of post-Discharge claims data available, the admission involved a same day transfer to or from another acute-care hospital	(81,11.7) (dementia diagnosis), (72.4, 14.5) (not dementia)	62.4 (dementia), 55.0 (not dementia)	2583	NO	ICD-9-CM	NO	NO

APACHE II = Acute Physiology and Chronic Health Evaluation II;  
ADL = Activities of Daily Living;  
CAM = Confusion Assessment Method;  
CGA= Comprehensive Geriatric Assessment;  
CIRS-G= Cumulative Illness Rating Scale-Geriatric;  
DEMQOL= Dementia Quality of Life measure;  
DRS = Delirium Rating Scale;  
DSM = Diagnostic and Statistical Manual of Mental Disorders;  
ICD= International statistical classification of disease;  
GDS = Geriatric Depression Scale;  
GHQ= General Health Questionnaire;  
IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly;  
MMSE = Mini-mental State Examination;  
SD = standard deviation;  
SIDAM= Kurz-SkalaStimmung/Aktivierung.

\*In Draper et al study, age range was >50, but the result was presented by age group. For our study, we just extracted the results from patients' age>65.

### **Prevalence and mortality of patients with Dementia/ Delirium/ Cognitive Impairments**

There were 7 papers that described prevalence of dementia, with the range from 2.6% to 43%(Table 1.2). Only 4 papers explored prevalence of delirium, with the range from 9% to 43%. Half of the included papers studied the prevalence of cognitive impairments, with a range of 19% to 48.6%.

Table 1.3describes mortality with dementia/delirium/cognitive impairments from each study. There were 6 studies assessing mortality of dementia in 30 days. Other papers also have description of mortality in 30 days, 6 months and 12 months+, but this did not involve more than 3 papers. I decided there was little sense in doing such a comparison with a small number of papers. It is also difficult in terms of heterogeneity. Finally, Idecided to conduct a Meta-analysis with papersthat study dementia and 30 days' mortality. Meta- analysis of 6 papers showed that people with dementia had significantly greater mortality by 11% (95%CI: 6%-16%,  $p<0.001$ , see Forest plot in Figure 1.2), compared with people without dementia, with significant heterogeneity ( $I^2=68\%$ ,  $p=0.01$ ).

There were 6 studies examined for the length of hospital stay for dementia/delirium/cognitive impairment students (Table 1.4). The longest stay was 26.1 days; the minimum length was 4.6 days. There were a totalof 5 studies with rehospitalisation rate of 30 days (27% and 17.8%), 6 months after admission (40%) and 12months after admission (59%).

*Table 1.2 Prevalence of delirium/dementia/cognitive impairment for patients aged 65+ in general hospital*

<b>Paper</b>	<b>Delirium % (95% CI), N</b>	<b>Dementia % (95% CI),N</b>	<b>Cognitive impairment % (95% CI),N</b>
①a. Sampson et al.(2009) UK, British Journal of Psychiatry	NA	42.4(38.5-46.3),261	47.9(43.96-51.84),296
①b. Sampson et al.(2013) UK, International Journal of Geriatric Psychiatry	NA	42.4(38.5-46.3),262	47.9(43.95,51.85),296
②Guijarro et al.(2010) Spain, Neuroepidemiology	NA	3.43→4.64 (from 1998 to 2003)(3.41-3.45→ 4.62-4.66), 5245→8209	NA
③Whittamore et al. (2014) UK, International Journal Of Geriatric Psychiatry	43(36.9- 49.1),107	43(36.85-49.15),106	48.6(42.39-54.81),121
④Kennedy et al. (2014) UK, Journal of the American Geriatrics Society	9(6.9-11.1),63	NA	NA
⑤Eeles et al. (2010) UK, Age and Ageing	37.1(31.4- 42.8),103	NA	NA
⑥Bickel et al. (2006) Germany, Dementia and Geriatric Cognitive Disorders	NA	NA	36.1(32.76-39.44),287
⑦Draper, B et al. (2011) Australia, International Psychogeriatric	NA	8(7.89-8.11),20034	NA
⑧Buurman, B et al. (2011) Netherland, PLoS ONE	40.1(36.3- 43.9),256	NA	19(15.96-22.04),118

Paper	Delirium % (95% CI), N	Dementia % (95% CI),N	Cognitive impairment % (95% CI),N
⑨Dodson,J.A. et al. (2013) USA, American Journal of Medicine	NA	NA	46.8(40.98-52.62),132
⑩Joray,MD et al. (2004) Switzerland, The American Journal of Geriatric Psychiatry	NA	NA	32.3(27.72-36.88),129
⑪Li Fang et al. (2013) China, Aging AND Experimental Research	NA	2.6(2.43-2.77),918	NA
⑫Daiello,L.A et al. (2014), USA, Archives and Gerontology and Geriatrics	NA	15.1(14.66-15.54),3908	NA
⑬Goldberg.SE et al. 2013 UK, BMJ(Online)RCT	NA	NA	NA

*Table 1.3 Mortality of delirium/dementia/cognitive impairment for patients aged 65+ in general hospital*

Confusion Condition	Paper	Mortality % (95%CI),N		
		30 Days(Index admission)	6 Months	12 Months+
Dementia	①a.Sampson et al.(2009) UK, British Journal of Psychiatry	18.1(15.06-33.16),47	NA	NA
	①b.Sampson et al.(2013) UK, International Journal of Geriatric Psychiatry	15(12.18-27.18),39	39.1 (33.1-45.0),102	48.3(42.2-54.4),126
	②Guijarro et al.(2010) Spain, Neuroepidemiology	19.3(19.26-38.56), 7813	NA	NA
	⑦Draper,B et al. (2011) Australia, International Psychogeriatric	8.3(8.19-16.49),3160	NA	NA

Confusion Condition	Paper	Mortality % (95%CI),N		
		30 Days(Index admission)	6 Months	12 Months+
	⑪Li Fang et al. (2013) China, Aging AND Experimental Research	9.8(9.49-19.29),90	NA	34.3(33.80-34.80),315
	⑫Daiello,L.A et al. (2014), USA, Archives and Gerontology and Geriatrics	8(7.67-15.67),313	NA	NA
	③Whittamore et al. (2014) UK, International Journal Of Geriatric Psychiatry	NA	37(31.00-43.00),40	NA
	④Kennedy et al. (2014) UK, Journal of the American Geriatrics Society	6(4.23-10.23),4	NA	NA



Confusion Condition	Paper	Mortality % (95%CI),N		
		30 Days(Index admission)	6 Months	12 Months+
	⑤Eeles et al. (2010) UK, Age and Ageing	35.9(30.26-66.16),37	NA	NA
Cognitive Impairment	①a.Sampson et al.(2009) UK, British Journal of Psychiatry	17.22(14.24-31.46),51	NA	NA
Cognitive Impairment		NA	37.5(33.68-41.32),132	45.7(41.77-49.63),161
	①b.Sampson et al.(2013) UK, International Journal of Geriatric Psychiatry			
	⑩Joray,MD et al. (2004) Switzerland, The American Journal of Geriatric Psychiatry	7(4.50-11.50),9	28.7(24.27-33.13),37	NA

Confusion Condition	Paper	Mortality % (95%CI),N		
		30 Days(Index admission)	6 Months	12 Months+
	⑬Goldberg.SE et al. 2013 UK, BMJ(Online)RCT	NA	25(21.5-28.46),71	NA

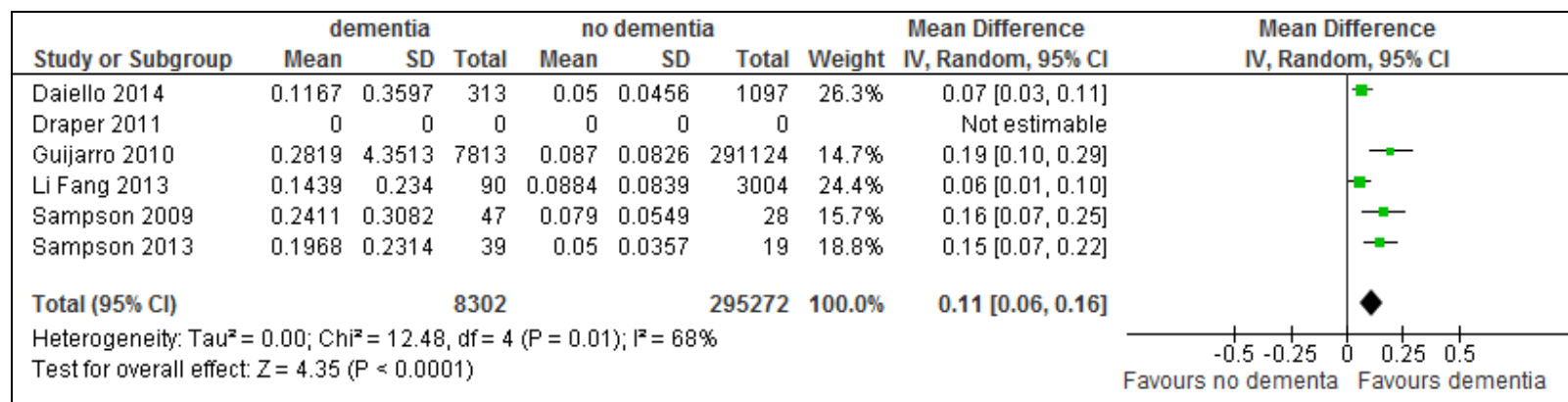


Figure 1.2Forest plot of mortality compared with dementia and no dementia.

*Table 1.4 Hospital stay days and rehospitalisation rate for patients with dementia / delirium / cognitive impairment*

<b>Paper</b>	<b>Hospital stay days</b>	<b>Rehospitalisation rate%</b>
<b>①a. Sampson et al.(2009) UK, British Journal of Psychiatry</b>	16.7	NA
<b>①b. Sampson et al.(2013) UK, International Journal of Geriatric Psychiatry</b>	16.7	NA
<b>②Guijarro et al.(2010) Spain, Neuroepidemiology</b>	13.4	NA
<b>③Whittamore et al. (2014) UK, International Journal Of Geriatric Psychiatry</b>	16	45 ( 6 months)
<b>④Kennedy et al. (2014) UK, Journal of the American Geriatrics Society</b>	4.6	27 (30 days)
<b>⑤Eeles et al. (2010) UK, Age and Ageing</b>	26.1	NA
<b>⑥Bickel et al. (2006) Germany, Dementia and Geriatric Cognitive Disorders</b>	20 (for the whole sample)	NA
<b>⑦Draper,B et al. (2011) Australia, International Psychogeriatric</b>	16.5	40(3 months)
<b>⑧Buurman, B et al. (2011) Netherland, PLoS ONE</b>	NA	NA
<b>⑨Dodson,J.A. et al. (2013) USA, American Journal of Medicine</b>	11	NA
<b>⑩Joray,MD et al. (2004) Switzerland, The American Journal of Geriatric Psychiatry</b>	NA	NA
<b>⑪Li Fang et al. (2013) China, Aging AND Experimental Research</b>	9	37.4(undetected impairment), 41.7(detected impairment)(no specified time)
<b>⑫Daiello,L.A et al. (2014), USA, Archives and Gerontology and Geriatrics</b>	13	NA
<b>⑬Goldberg.SE et al. 2013 UK,</b>	6.7	17.8(30 days)

### **1.3.6 Discussion**

#### **Prevalence of confusion status**

The studies in the review have covered patients across 6 countries, including Europe, North America, Australia and Asia. So the results can be seen as representing the general condition of confusion for the elderly worldwide. The lowest prevalence of delirium was reported by Kennedy et al (20), with just 9%. His study was a prospective observational cohort study conducted in urban tertiary care emergency department (ED). The highest prevalence of delirium was 43% which was reported by Whittamore et al. (19). This study was conducted in an acute geriatric medical ward, trauma orthopaedic ward and general medical ward, with the population older and more female, which may cause the prevalence of dementia to be higher than other papers. In addition, they used DRS-R-98 as tools to diagnosis delirium. Compared to other scales, DRS-R-98 were more sensitive (91% to 100%) to differentiate delirium from dementia and depression and usually can be taken over a period (30, 31). The high sensitivity of the DRS-R-98 may cause the risk of making a false positive diagnosis, which may cause the high prevalence of this study (32). The lowest prevalence for dementia was reported as 2.6%. This study was a case-control study conducted over 10 years within a Neurology department of a tertiary hospital setting. The highest prevalence of dementia was reported by Sampson et al. (16), whose study was conducted among patients much older (>70 years old). Also the patients with delirium were excluded during the sample selection, which may cause the population so focused, to lead to a high prevalence.

#### **The measurement tools of the studies**

Each investigator of the studies must use some tools to avoid the misclassification between one confusion status and another. Hardly any study explored dementia, cognitive impairment nor delirium all together. That maybe because of the difficulties in defining three confusion states clearly during diagnosis. Since each study had different background setting, various instruments had been used for assessing different confusion states. The most prevalent tools used among these studies to explore delirium was CAM (33), which is believed to have high specificity, accurate, concise and easy to conduct by clinicians (31). The tools which were used to

screen for dementia varied among the included articles. DSM(14) was the most common one; ICD (34) was also used by some papers for dementia diagnosis. The MMSE was the most common tools used for assessing CI, accounting for 90% of the papers which have screening CI. This result was almost the same as a survey of assessment scales in Old Age Psychiatry services in England and Northern Ireland(35). In that survey, approximately 95% of the responds used the MMSE (15) as the cognitive screening instruments.

### **Outcomes of the study**

The mortality of each kind of confusion state was only reported by one or more studies, still fewer that reported 30 days' mortality, 6 months' mortality and 12 month' mortality. So it was difficult to make general conclusions with all the individual forms of confusion state. I can just draw conclusions from the Meta-analysis result of 30 days' mortality which was that the 30 days' mortality of people with dementia indeed had higher mortality than people with no dementia. As many studies did not report the outcome (length of stay, readmission rate etc.) for those with no confusion, Meta-analysis was difficult to be conducted with these outcomes. In Kennedy's (20) paper, length of stay days was apparently shorter than other papers. Since the patients who admitted to tertiary hospital's ED may be in much more serious condition than others in general hospital, and was more likely to discharge quickly to an intensive care facility.

### **Limitations**

This systematic review may be limited by the small number of identified studies and its inclusion of articles printed only in English. As many included papers did not report the outcomes for people with no confusion, comparison and conclusion are difficult to make. Besides, this review was only conducted by 2 researchers, which may cause biases in selection and evaluation of the papers. Although the settings of the inclusion papers had been limited to general hospitals, the settings and admitted patients may be varied among community and countries and heterogeneity measured by I squared was high. So the conclusion may make more sense when all the diversity is taken into account. As I include both the Sampson's paper in, which

may mix some factors which may influence the results. Some papers used tools to select the patients with single condition. This may reduce the representativeness of the results. More compatible quality assessment tool should be adopted within the systematic review.

### **1.3.7 Future Work**

If meta-analysis were doing again in retrospect, we might have only included one of these papers. However, for this project we would not do this again. To understand more about the relationship of final outcomes and confusion status of the patients, I conducted a data analysis with a dataset derived from a routine programme in a general hospital in Fife. This dataset will cover the whole population of Fife, which would be more representative. In addition to the description of people's characteristics, I will also conduct survival analysis for all-cause mortality controlled by adjusting for many factors (demographic factors, social factors and co-morbidity) using Cox's regression model. In addition, as two kinds of the most prevalent causes of death among the elderly, the relationship between cardiovascular / respiratory death and confusion status will be explored together in my later analysis. The assumption of proportional hazards in these models will also be explored.

## 2. Methods

### 2.1 Setting

The population is derived from Fife NHS Health Board on the east coast of Scotland. It is located between the Firth of Tay and the Forth, which is divided into three districts, Dunfermline, Kirkcaldy and North-East Fife(36). The region map can be seen from Appendix 2. Fife is the third largest local authority area of Scotland by population of just under 367,000. There are two main hospitals in Fife, Victoria Hospital in Kirkcaldy and Queen Margaret Hospital in Dunfermline (37). As the main data sources for the study, the Victoria Hospital in Kirkcaldy was opened in January 2012 and housed all emergency admissions in NHS Fife.

### 2.2 Dataset and Participants

The data comes from the Cognitive Geriatric Assessment research (CGA) programme, which was a retrospective cohort study conducted with Older Persons Acute Assessment (OPRAA) dataset which already existed. From 2009, NHS Fife has performed a pilot project to evaluate the impact of standardised Acute Comprehensive Geriatric Assessment (A-CGA) among patients over 65 years who were admitted into the Victoria Hospital. Over time, the A-CGA obtained a positive feedback from the patients' families and carers. It has also been noticed that the identification of undiagnosed dementia has increased. As a result, NHS Fife decided to adopt OPRAA which was designed based on A-CGA as a routine clinical identification from April 2011. One questionnaire was used to investigate the patients' functional and cognitive ability, screen for delirium, and document their socio-environmental situation. Patients aged above 65 years' old who have an admission to acute hospital (except patients with a predicted length of stay less than 24 hours, a poor prognosis or acute illness) are required to take OPRAA by trained specialist nurses. All the results of assessment are recorded electronically which can be uploaded and are curated by the Health Informatics Centre (HIC) in Dundee

University(38). Before the analysis, all the dataset has been cleared by one statistician for the feasibility of the analysis.

The OPRAA dataset currently holds over 13000 admission records and is being updated every week. The routine assessment questionnaire can be seen from Appendix 3. Apart from Fife OPRAA dataset, the CGA program also took advantage of other datasets hosted by HIC for analysis; such as the general registrar office (GRO) death dataset, the Scottish Morbidity Records 01(SMR01) dataset and the patient-level community dispensed prescribing dataset.

For this study, the group of interest was the OPRAA records of patients aged 65 years or more who were admitted to Fife Victoria hospital between 01 January 2012 and 31 December 2012. If more than one visit was recorded, the first admission was used. These participants' data were followed up until 30 September 2013. So the maximum follow up length would be 21 months. In addition, we also linked the SMR01 dataset, GRO dataset and the master Community Health Index (CHI) dataset held by HIC (38)for analysis. The group for control in the statistical models would be the patients who also admitted in Victoria hospital but did not have the confusion problems.

- SMR01 data will also be used to calculate Charlson Comorbidity Index (CCI) (39-43).
- GRO data will be used to obtain the participant's death data and to calculate survival time within the follow-up period, and to obtain the causes of death.
- Anonymised CHI(ProCHI) data will be used to get patient's demographic details including age, sex, Scottish Index of Multiple Deprivation score (SIMD)(44) .

## 2.3 Covariates and Definitions

### Pro-CHI

The Pro-CHI is generated by the HIC Data Analyst to uniquely anonymise a typical NHS dataset with the standard patient-identifiable CHI number. There are



also 10 digits for the Pro-CHI. The first 3 digits are character and the last 7 are integers.

### **Dementia**

Dementia in OPRAA referred to diagnosis which was done by specialist memory clinics who are in charge of initiating drugs to treat dementia. In other words, diagnosed dementia participants were people who had a pre-admission diagnosis record or received any licenced drug for the treatment of dementia. Those with no such record on admission to Victoria hospital were coded as zero for no dementia.

### **General clinical delirium**

Admissions with accompanying drowsiness with a change from usual function or activity can be treated as general clinical delirium. In addition, clinical history suggestive of delirium also would be classified into general clinical delirium. Those patients who were also admitted in the same hospital but without drowsiness or a clinical delirium history would be coded as zero for no general clinical delirium.

### **Fully syndromic delirium (FSD)**

The lack of uniform diagnostic criteria and frequently presented nonspecific delirium among the elderly has resulted in poor clinical management and study of delirium. Delirium is often overlooked or misdiagnosed as depression or psychosis, as in one study, only 35% of delirium cases were truly recognized by physicians(45). Considering the complexity and difficulty of a diagnosis of delirium, the Confusion Assessment Method (CAM) score was specified and used to define the fully syndromic delirium(33). The CAM includes two parts. Part one is an assessment instrument which contains 9 questions to evaluate overall cognitive impairment. Part two includes four distinguishing features which can apparently identify delirium or reversible confusion from other types of cognitive impairment. The diagnosis of delirium required the presence of both first and second features and of either the third or the fourth feature. FSD is a more definitive diagnosis of delirium than general

clinical delirium. Those patients who were also admitted to the Victoria hospital but were negative to the CAM assessment were coded as zero for no FSD.

### **Cognitive impairment (CI)**

The population with cognitive impairment was defined as having Abbreviated Mental Test (AMT) score of 7 or less on admission(46, 47). With ten questions, the AMT was first introduced in 1972, which is probably the most well-known test in general hospital use. Those patients who were also admitted to the Victoria hospital with the AMT score above 7 were defined as having no CI.

### **CCI**

The CCI is the most commonly used score to summarise comorbidity for patients according to the International Classification of Disease, 10th Revision (ICD-10) (34). Adjusting for risk of mortality or resource use, each kind of comorbidity has different score weight. The CCI is the sum of all the weights of a patient. For example, a score of zero means there is no comorbidity found for the patient. With the CCI increasing, the risk of death will also increase or more resource will be used(39). In this study, the original CCI has been recoded into 4 categories: score 0, score 1-2, score 3-4, and score 5+.

### **The cause of death**

The international statistical classification of disease and related health problems 10<sup>th</sup> revision (ICD-10)(34) were used for classification of cause of death. ICD records of J00-J99 were diagnosis of disease of the respiratory system (Respiratory) and I00-I99 were diagnosis of disease of the circulatory system (CVD). In this study, only these two causes of mortality were explored in addition to all-cause mortality.

### **Demography**

The demographic variables included gender, age and SIMD. SIMD is the Scottish Government's official tool for identifying those places in Scotland suffering from deprivation(44). It incorporates seven different domains of deprivation (Employment; Income; Health; Education, Skills and Training; Geographic Access to Services; Crime; Housing), combining them into a single index. SIMD has divided

Scotland into 6,505 small areas, called data zones, each containing around 350 households. The Index provides a relative ranking for each data zone, from 1 (most deprived) to 5 (least deprived). For my analysis, I looked the SIMD with ranks to quintiles, which splits the data zones into 5 groups, each containing 20% of the whole Scotland's data zones (Table 2.1). The local SIMD summary for Fife published in 2012 can be seen from theAppendix4.

*Table 2.1SIMD ranks to quintiles*

<b>SIMD Rank</b>		
Quintile (20%)	From	To
1	1	1301
2	1302	2602
3	2603	3903
4	3904	5204
5	5205	6505

## 2.4 Outcomes

The main outcome of the study was the survival time for all-cause mortality of each patient. Survival time was the result of the patient's registered death date subtracted from the admission date. For the patients who were still alive until the end date of the follow-up; I censored them at 30 September 2013 to subtract admission date to get a censored survival time for analysis.

## 2.5 Data Management and Ethics

The data for study was all supported by Health Informatics Centre (HIC) Services(38), which is a University of Dundee research support unit within Tayside Academic Science Collaboration (TASC) and the Farr Institute, in collaboration with NHS Tayside and NHS Fife. HIC Services supports high impact research through the collection and management of high quality data. The environment which HIC Services provides is within a "Safe Haven", which has strong governance for the provisioning of data to academics and other users. In this model, data are not released externally to data users for analysis on their own computers but placed on a server at HIC, within a restricted and secure IT environment.

The Community Health Index (CHI) is a unique population register number which was generally used in NHS(48). To maximise data security and data subject confidentiality, HIC anonymises the data used for research using a project specific

anonymised Pro-CHI. Each Pro-CHI is generated by the HIC Data Analyst to uniquely anonymise a typical NHS dataset CHI number(38).

The datasets which analysed for this study were complete datasets after cleaning, which hopefully represented 80% of all the potential admissions.

Research use was with the consent of the NHS Fife Caldicott Guardian based on researcher access only to anonymised data in a secure Safe Haven that does not permit data export. The dataset will be linked subject to HIC Standard Operating Procedures, which have been reviewed by the NHS Tayside Research Ethics Service.

## 2.6 Data Analysis

The data were analysed by four age groups: 66-75 years; 76-85 years; 86-95 years; and 96 years and over. The analyses were conducted using SAS version 9.3 provided by the server of the Safe Haven of HIC. Descriptive analyses of patients' characteristics were described in terms of frequencies, percentages for categorical variables, means and standard deviations (SD) for continuous variables. Characteristic differences across the people with dementia and no dementia, CI and no CI, clinical delirium and no clinical delirium, FSD and no FSD were checked for significance using  $\chi^2$  tests and ANOVA tests. In order to describe the distribution of survival times and test differences in survival between different age groups, gender, CCI, SIMD and disease groups, Kaplan-Meier procedures and Log-Rank Tests were conducted. The starting point was a specific admission date between 01 January 2012 to 31 December 2012, and the end of the follow-up period was 30 September 2013. The event of interest was all-cause death. Survival times of patients who were still alive were censored at the end of the follow-up time on 30 September 2013. The median survival time and 95% confidence intervals (95% CIs) would be used to summarise the distribution of survival times. The median survival time is stated as the time half of the patients are expected to survive. Log-Rank tests with a result of  $p < 0.05$  illustrated the significance of differences in survival time between the groups. Cox's proportional hazards regression model was also employed to investigate the association between death and survival time with multiple predictors. Backward elimination method was used for modelling adjusted age group, gender, SIMD, CCI

and variables of cognition status. To check the validity of the survival model, Kolmogorov-Type Supremum Tests (49) with the 'assess' statements in SAS were also added in the final model. The 'assess' statement used the graphical and numerical method for checking the adequacy of the Cox regression model. This method is derived from cumulative sums of martingale residuals over follow-up times or covariate values. The results of  $p > 0.05$  for this test would represent the assumption of proportional hazards was satisfactory in the established model. Cox's model and Kaplan-Meier plots were also employed to check the relationship between Respiratory and CVD mortality and the four variables of cognition status adjusted for other factors. Some of the key SAS code for the study can be seen from Appendix 5.

## 3. Results

### 3.1 Characteristics of Patients

During the follow-up period, there were a total of 4780 patients with age 65+ years on admission. Characteristics of these patients are shown in Table 3.1. The mean age was 81.5 years with a standard deviation of 8.0 and 56% (2678) of patients were female. The median survival time was 355 days. According to the records, clinical delirium and CI were the two most prevalent diagnoses, with 22.8% (1089) and 16.7% (796) respectively. Only less than 10% of patients were diagnosed as having dementia or FSD respectively (8.6%, 413 for dementia; 6.6%, 317 for FSD). 23.6 % (1127) of the patients were found to come from the most deprived postcode sectors in Scotland. Over 50 % (50.8%, 2429) of patients have a CCI between 1 and 2. The all-cause mortality was 34.4 % (1643), among the patients who have died, 6% (288) of them died due to respiratory condition and 9.2% (441) as a result of CVD.

Table 3.2 and Table 3.3 indicate the results of bivariate comparisons between each specified confusion condition group and no condition cases. Each condition group was from an older population (means 86.2 versus 81.0 for dementia; 83.7 versus 80.8 for clinical delirium; 85.3 versus 81.2 for FSD; 85.4 versus 80.7 for CI;  $p < 0.01$  for differences). Females accounted for a higher percentage for each condition group (64.4% for dementia; 57.3% for clinical delirium; 60.3% for FSD; 60.8% for CI), even though the gender difference between clinical delirium /CI and no delirium /CI group was not statistically significant. CCI was found to significantly differ between people with the condition and no condition group except for FSD ( $p < 0.05$ ), with most of the population score 1 to 2 in CCI for every group. Apart from dementia, the other three condition groups all have significant differences in distribution of mortality from CVD compared with the no condition population ( $p < 0.05$  for differences).

*Table 3.1 Baseline characteristics of the total population*

		Total population (N=4780)
<b>Age, years, mean± SD</b>		81.5±8.0
<b>Female,%(N)</b>		56(2678)
<b>Dementia,%(N)</b>		8.6(413)
<b>Clinical delirium,%(N)</b>		22.8(1089)
<b>FSD,%(N)</b>		6.6(317)
<b>CI,%(N)</b>		16.7(796)
<b>SIMD,%(N)*</b>	0-20% Most deprived	23.6(1127)
	20-40%	27.8(1330)
	40-60%	23.2(1108)
	60-80%	13.8(659)
	80-100% Least deprived	11.6(554)
<b>CCI,%(N)</b>	0	26.8(1283)
	1-2	50.8(2429)
	3-4	14.8(709)
	5+	7.5(359)
<b>Survival time, days, median± SD</b>		355±185.8
<b>All-cause mortality,%(N)</b>		34.4(1643)
<b>Respiratory mortality,%(N)</b>		6.0(288)
<b>CVD co-mortality,%(N)</b>		9.2(441)

SD: standard deviation;

FSD: Fully syndromic delirium;

CI: Cognitive impairment;

SIMD: Scottish Index of Multiple Deprivation score;

CCI: Charlson Comorbidity Index;

RESP: Disease of the respiratory system;

CVD: Disease of the circulatory system.

\* SIMD data missing for 2 patients.



*Table 3.2 Characteristics of the patients with dementia/CI and bivariate comparisons between disease groups*

		<b>Dementia</b>		<b>P*</b>	<b>CI</b>		<b>P*</b>
		Yes N=413	No N=4367		Yes N=796	No N=3984	
<b>Age, years</b>		86.2±6.7	81.0±8.0	<0.01	85.4±7.3	80.7±7.9	<0.01
<b>mean± SD</b>							
<b>Female,%</b>		64.4	55.2	<0.01	60.8	55	<0.01
<b>(N)</b>		(266)	(2412)		(484)	(2194)	
<b>SIMD,%</b>	Rank			0.52			0.04
<b>(N)**</b>	0-20% Most deprived	20.1 (83)	24 (1044)		27.5 (219)	22.8 (908)	
	20-40%	28.6 (118)	27.8 (1212)		27.4 (218)	28 (1112)	
	40-60%	24 (99)	23.1 (1009)		22.1 (176)	23.4 (932)	
	60-80%	14.8 (61)	13.7 (598)		11.7 (93)	14.2 (566)	
	80-100% Least deprived	12.6 (52)	11.5 (502)		11.3 (90)	11.7 (464)	
<b>CCI,%</b>	Rank			<0.01			0.07
<b>(N)</b>	0	7.3 (30)	28.7 (1253)		25.1 (200)	27.2 (1083)	
	1-2	69.0 (285)	49.1 (2144)		51.3 (408)	50.7 (2021)	
	3-4	21.6 (89)	14.2 (620)		17.3 (138)	14.3 (571)	
	5+	2.2 (9)	8.0 (350)		6.3 (50)	7.8 (309)	
<b>Respiratory co-mortality, %</b>		7.5	5.9	0.19	6.4	6.0	0.62
<b>(N)</b>		(31)	(257)		(51)	(237)	
<b>CVD co-mortality, %</b>		11.1	9.1	0.16	13.3	8.4	<0.01
<b>(N)</b>		(46)	(395)		(106)	(335)	

SD: standard deviation;

FSD: Fully syndromic delirium;

CI: Cognitive impairment;

SIMD: Scottish Index of Multiple Deprivation score;

CCI: Charlson Comorbidity Index;

CVD: Disease of the circulatory system.

\* Chi-square test (for categorical variables) or ANOVA (for continuous variables) comparing subjects with dementia to no dementia; CI to no CI.

\*\* SIMD data missing for 2 patients.

*Table 3.3 Characteristics of the patients with clinical delirium/FSD and bivariate comparisons between disease groups*

		<b>Clinical delirium</b>		<b>p*</b>	<b>FSD</b>		<b>p*</b>
		Yes N=1089	No N=3691		Yes N=317	No N=4463	
<b>Age, years</b>		83.7±7.6	80.8±8.0	<0.01	85.3±7.0	81.2±8.0	<0.01
<b>mean± SD</b>							
<b>Female,%</b>		57.3	55.7	0.33	60.3	55.7	0.12
<b>(N)</b>		(624)	(2054)		(191)	(2054)	
<b>SIMD,%</b>	Rank			0.94			0.43
<b>(N)**</b>	0-20,%	23.4	23.7		22.1	23.7	
	Most	(254)	(873)		(70)	(1057)	
	deprived						
	20-40%	23.2	27.7		26.8	28	
		(309)	(1021)		(85)	(1245)	
	40-60%	23.3	23.2		25.9	23	
		(253)	(855)		(82)	(1026)	
	60-80%	14.1	13.7		15.8	13.7	
		(153)	(506)		(50)	(609)	
	80-100%	11	11.8		9.5	11.8	
	Least	(119)	(435)		(30)	(524)	
	deprived						
<b>CCI,%</b>	Rank			<0.01			0.56
<b>(N)</b>	0	23.3	27.9		28.7	26.7	
		(254)	(1029)		(91)	(192)	
	1-2	52.0	50.5		47	51.1	
		(566)	(1863)		(149)	(2280)	
	3-4	18.0	13.9		16.4	14.7	
		(196)	(513)		(52)	(657)	
	5+	6.7	7.8		7.9	7.5	
		(73)	(286)		(25)	(334)	
<b>Respiratory co-</b>		7.3	5.7	0.05	7.3	6.0	0.34
<b>mortality,%</b>		(79)	(209)		(23)	(265)	
<b>(N)</b>							
<b>CVD co-</b>		13.4	8.0	<0.01	14.5	8.9	<0.01
<b>mortality,%</b>		(146)	(295)		(46)	(395)	
<b>(N)</b>							

SD: standard deviation;

FSD: Fully syndromic delirium;

CI: Cognitive impairment;

SIMD: Scottish Index of Multiple Deprivation score;

CCI: Charlson Comorbidity Index;

CVD: Disease of the circulatory system.

\* Chi-square test (for categorical variables) or ANOVA (for continuous variables) comparing subjects with clinical delirium to no clinical delirium; FSD to no FSD.

\*\* SIMD data missing for 2 patients.

### 3.2 Analysis of Median Survival Time and Kaplan-Meier Survival Curves

In total, there were 1643 patients who died between 01 January 2012 and 30 September 2013. Among the cases, there were always over 40% mortality no matter which condition group the patients belonged to. Log-Rank tests highlighted that there were significant differences of mortality between age group, gender, CCI and four condition groups ( $p \leq 0.01$ ) (Table 3.4). However, the mortality was shown to be similar with different SIMD groups. Median survival time can only be observed with age group 95+ (345 days), dementia group (544 days), FSD group (541 days) and CCI 5+ group (61 days).

*Table 3.4 Log-Rank test and median survival time for the patients dead with all-cause*

		Median survival time, days(95%CI)	Death,%(N)	Log-Rank P-value
<b>Age group</b>	66-75	NA	25.4(319)	<0.01
	76-85	NA	23.1(641)	
	86-95	NA	42(602)	
	95+	345(210,NA)	52.3(81)	
<b>Gender</b>	Male	NA	37.2(862)	<0.01
	Female	NA	32.2(781)	
<b>Dementia</b>	Yes	544(455,NA)	45(186)	<0.01
	No	NA	33.4(1457)	
<b>Clinical delirium</b>	Yes	NA	42(457)	<0.01
	No	NA	32.1(1186)	
<b>FSD</b>	Yes	541(363,NA)	48(152)	<0.01
	No	NA	33.4(1491)	
<b>CI</b>	Yes	NA	43.2(344)	<0.01
	No	NA	32.6(1299)	
<b>CCI</b>	0	NA	21.9(281)	<0.01
	1-2	NA	31.5(766)	
	3-4	NA	43(305)	
	5+	61(50,78)	17.7(291)	
<b>SIMD*</b>	0-20% Most deprived	NA	33.3(375)	0.43
	20-40%	NA	34.7(462)	
	40-60%	NA	36(399)	

	Median survival time, days(95%CI)	Death,%(N)	Log-Rank P-value
60-80%	NA	34.9(230)	
80-100%Least deprived	NA	31.8(176)	

\* SIMD data missing for 2 patients

Graphical assessment of survival probability between groups and other patients using the Kaplan-Meier survival curves can be seen from Figure 3.1 to Figure 3.8. The differences mentioned above remained in the curves. Even though some of the median survival times were not available from the previous analysis, four survival curves (Figure 3.1-Figure 3.4) all illustrate that no condition group always had a better survival probability in terms of survival days than the condition group, also with a significant trend for age group (Figure 3.5). Figure 3.6 and Figure 3.7 indicate that either patients with more comorbidity or male patients have poorer survival than patients with less comorbidity or female. The mortality of those patients with different SIMD differed slightly, but these differences were not significant, which can also be observed from Figure 3.8.

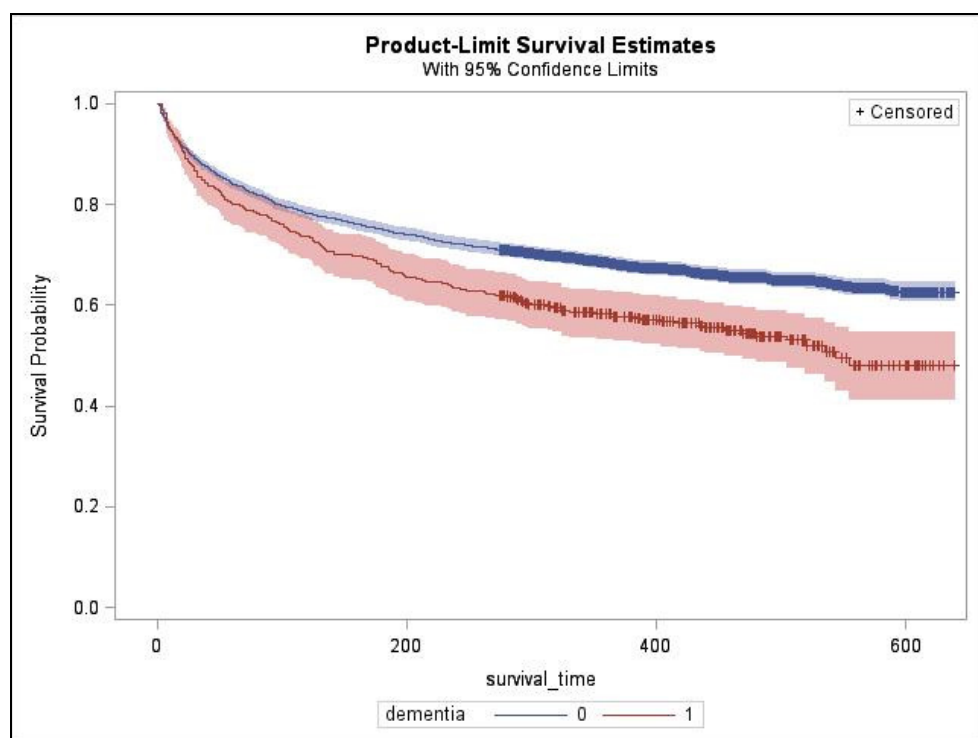


Figure 3.1 Kaplan-Meier survival Curves of all-cause mortality for patients with and without dementia (0: no dementia; 1: dementia).

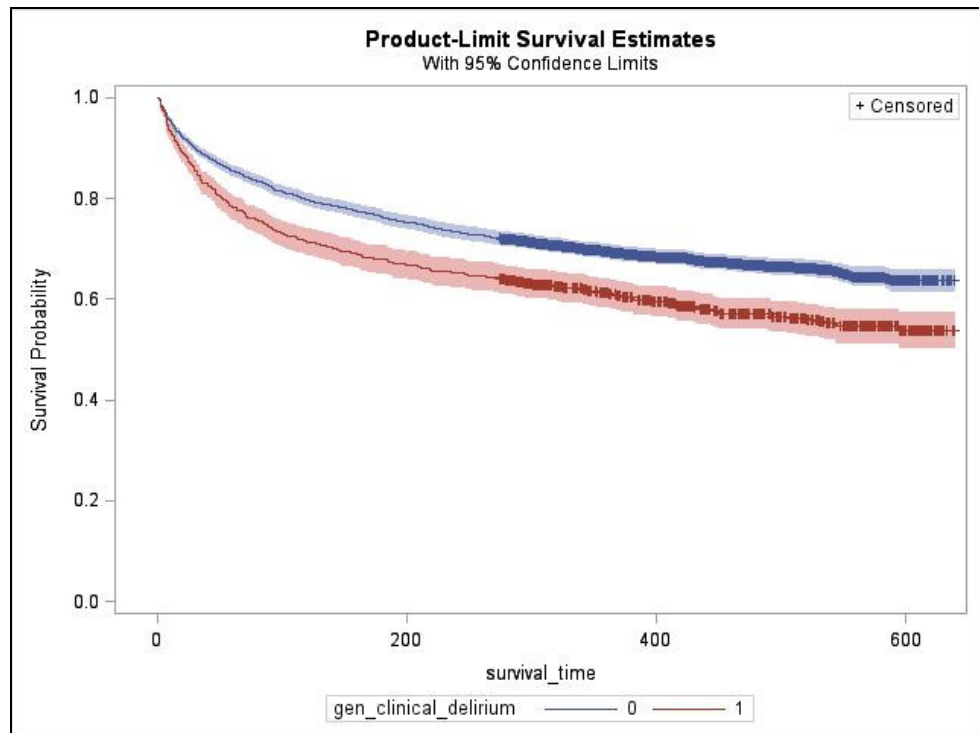


Figure 3.2 Kaplan-Meier survival Curves of all-cause mortality for patients with and without clinical delirium (0: no clinical delirium; 1: clinical delirium).

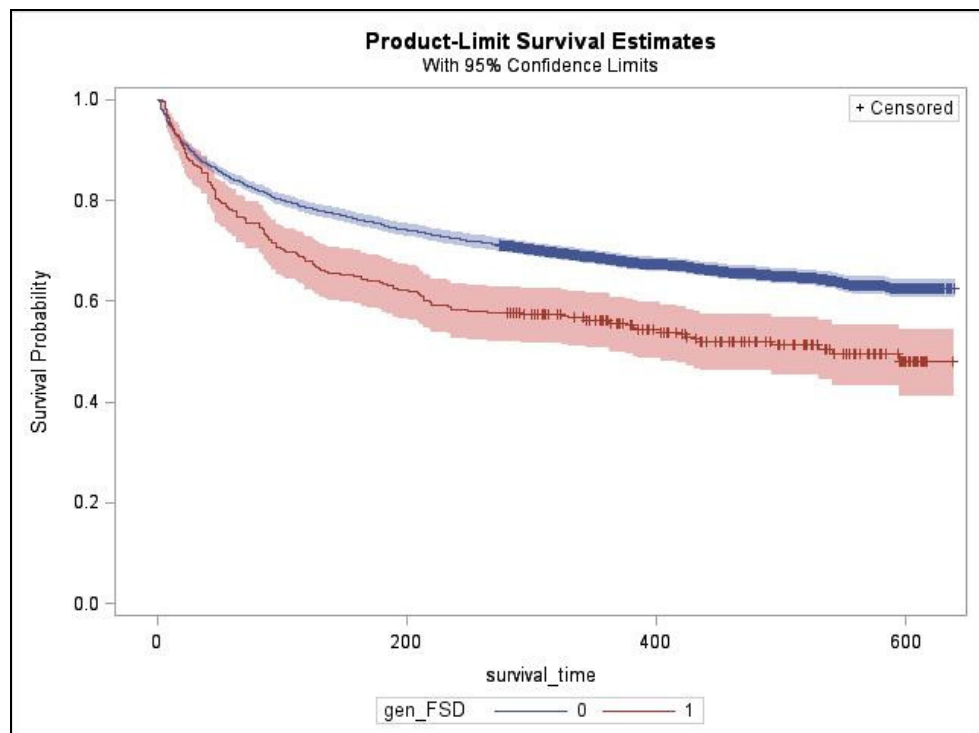


Figure 3.3 Kaplan-Meier survival Curves of all-cause mortality for patients with and without FSD (0: no FSD; 1: FSD).

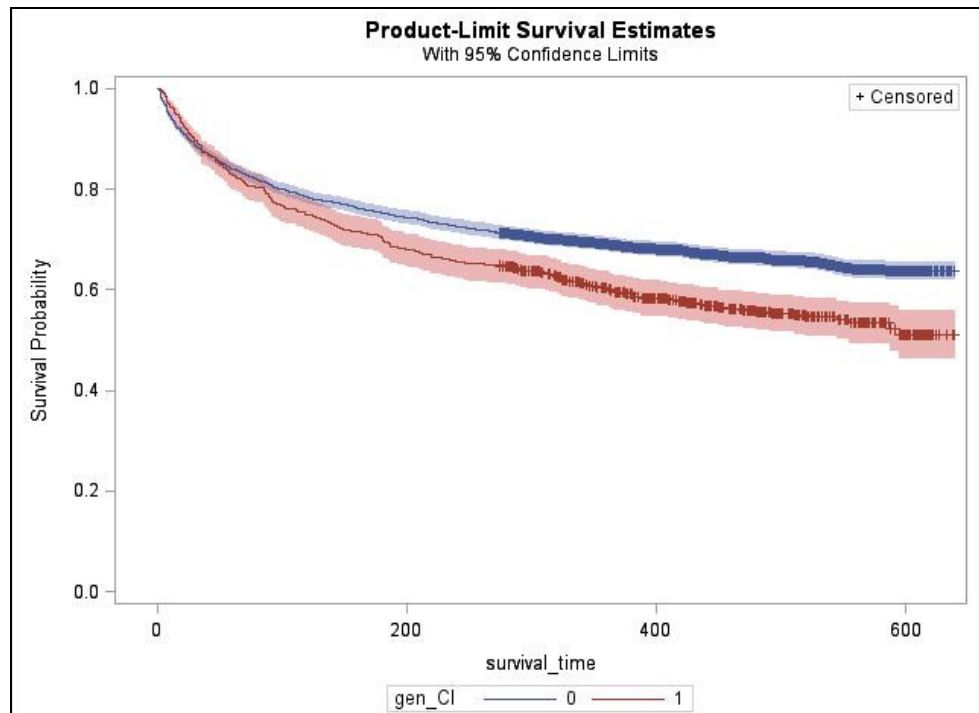


Figure 3.4 Kaplan-Meier survival Curves of all-cause mortality for patients with and without CI (0: no CI; 1: CI).

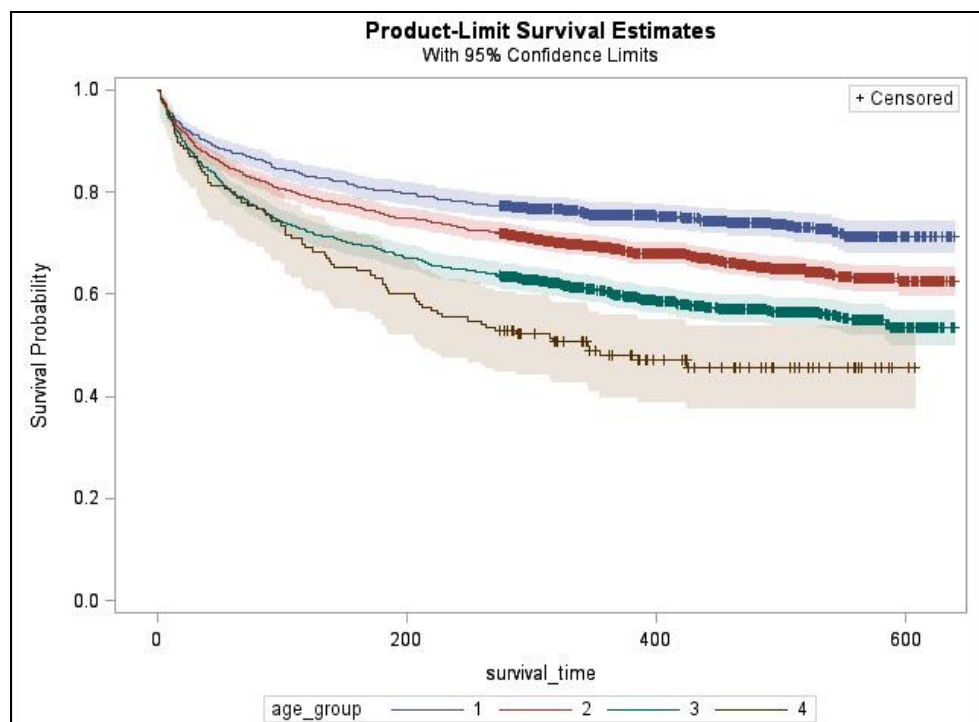


Figure 3.5 Kaplan-Meier survival Curves of all-cause mortality for patients with different age groups (1: 66-75 years old; 2: 76-85 years old; 3: 86-95 years old; 4: 95+ years old).

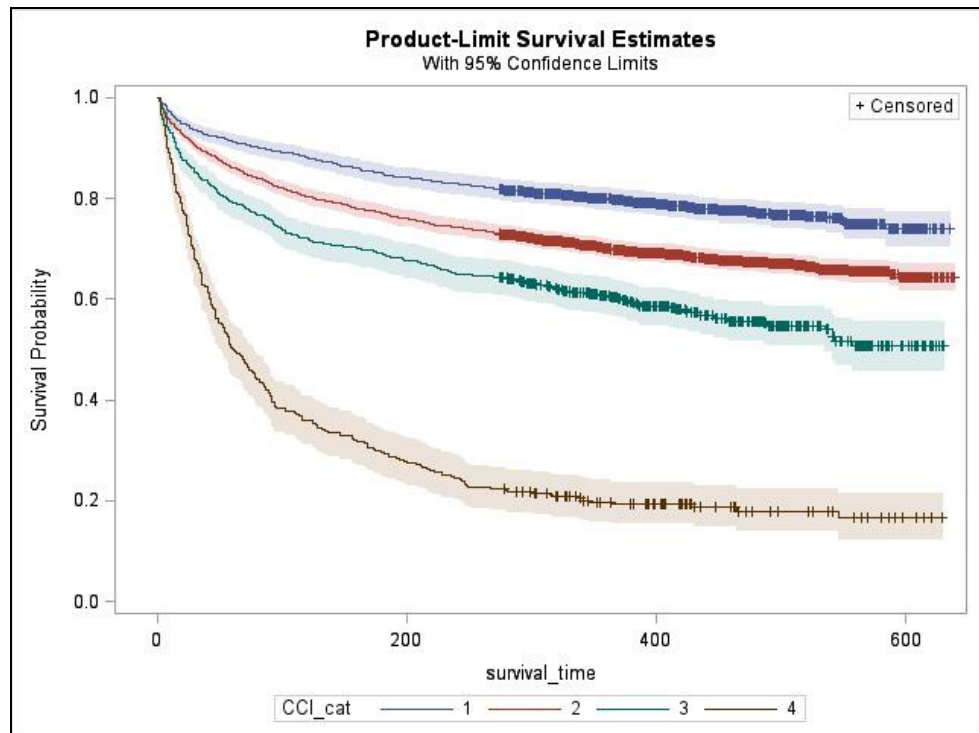


Figure 3.6 Kaplan-Meier survival Curves of all-cause mortality for patients with different CCI groups (1: score 0; 2: score 1-2; 3: score 3-4; 4: score 5+).

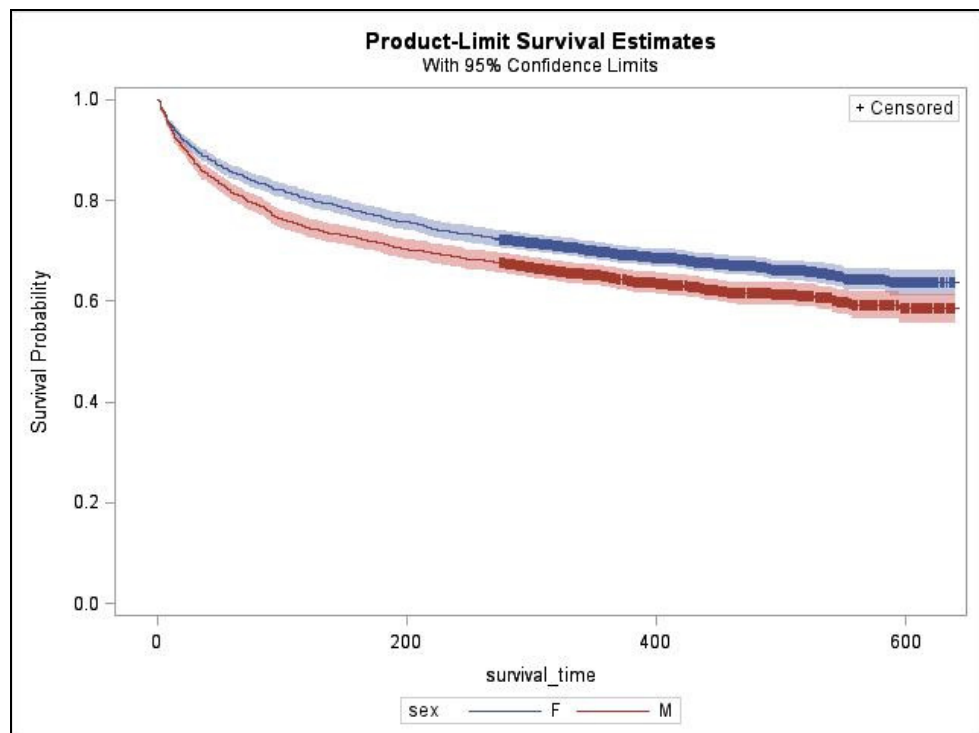


Figure 3.7 Kaplan-Meier survival Curves of all-cause mortality for patients with each gender.



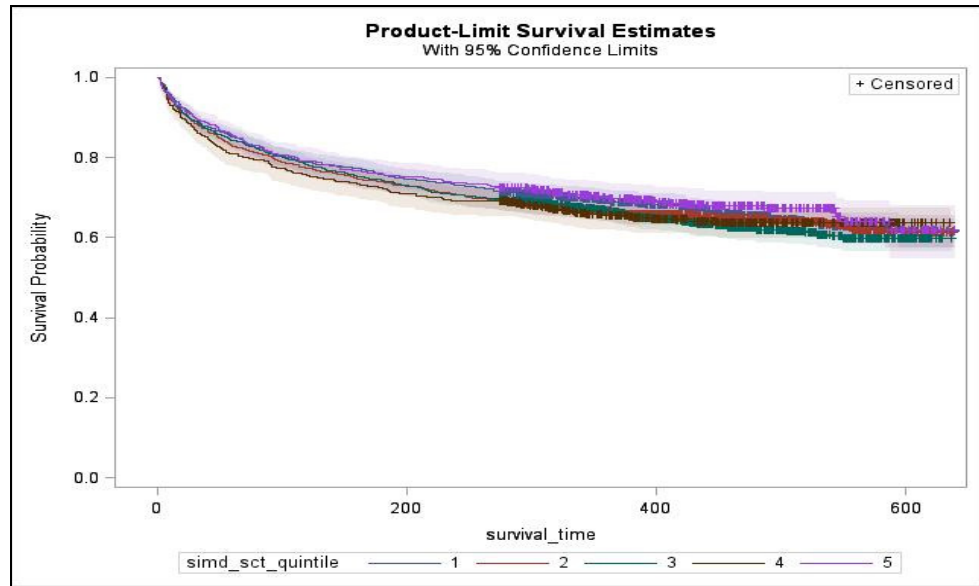


Figure 3.8 Kaplan-Meier survival Curves of all-cause mortality for patients with different SIMD (1: most deprived; 2: 20-40% deprived; 3: 40-60% deprived; 4: 60-80% deprived; 5: 80-100% least deprived).

### 3.3 Mortality for 30 Days, 6 Months and 12Months

There were no large differences between mortality for people with and without each condition (Table 3.5). Compared with no condition, each type of condition had significantly higher 6 months' mortality ( $p < 0.01$ ). The maximum difference was seen with FSD and no FSD, which reached up to 11.5%. There were no significant differences between dementia and no dementia in 30 days' and 12 months' mortality, even though the mortality was indeed higher for dementias.

*Table 3.5 Comparison tables of 30 days, 6 months and 12 months mortality for confusion patients with no confusion patients*

	30 days' mortality %(N)	P*	6 months' mortality %(N)	P*	12 months' mortality %(N)	P*
<b>Dementia VS. No dementia</b>	13.3(55)	0.12	32.2(133)	<0.01	55.69(230)	0.06
	10.8(472)		24.9(1089)		50.77(2217)	
<b>Clinical delirium VS. No clinical delirium</b>	14.4(157)	<0.01	32.1(349)	<0.01	53.26(580)	0.12
	10.0(370)		23.7(873)		50.58(1867)	
<b>FSD VS. No FSD</b>	12.9(41)	0.26	36.3(115)	<0.01	53.94(171)	0.31
	10.9(486)		24.8(1107)		51.00(2276)	
<b>CI VS. No CI</b>	10.3(82)	0.48	29.9(238)	<0.01	51.01(406)	0.91
	11.2(445)		24.7(984)		51.23(2041)	

\* Chi-square test

### 3.4 Cox's Regression Model for All-cause Mortality

Table 3.6 shows the results of Cox's regression model. In unadjusted Cox's model, the hazard of death was associated with dementia, clinical delirium, FSD and CI as well as some demographic factors. When adjusting for the four disease conditions, age, gender, CCI and SIMD, the hazard of death for patients with dementia was estimated to decrease slightly from 1.42 to 1.17 with a 95% confidence interval of 1.00 -1.38 . Similarly, those with clinical delirium had 1.23 times greater hazard ratio (HR) to death (95% CI: 1.10-1.37) which also declined from 1.39 when no factors were adjusted for. Although FSD and CI were shown to significantly increase the risk of death with hazard ratios of 1.53 and 1.35 by themselves, they were not significant predictors anymore in the adjusted model. Age, male gender and CCI always significantly contributed to predicting the hazard of death no matter what was adjusted for. With age and CCI increasing, the hazard of death also rose. Besides, there would be about 20% increase for mortality if the patient was male in

adjusted model. SIMD was shown to be non-significant with hazard of death neither individually nor in the multiple variables regression model.

*Table 3.6 Hazard ratios for all-cause mortality from Cox's regression model, with adjustment for all variables*

		Unadjusted			Adjusted		
		HR	95%CI	P-value	HR	95%CI	P-value
<b>Dementia</b>		1.42	1.22-1.66	<0.01	1.17	1.00-1.38	<0.05
<b>Clinical delirium</b>		1.39	1.25-1.55	<0.01	1.23	1.10-1.37	<0.01
<b>FSD</b>		1.53	1.30-1.81	<0.01			
<b>CI</b>		1.35	1.20-1.52	<0.01			
<b>Age group</b>	66-75	1			1		
	76-85	1.34	1.18-1.54	<0.01	1.34	1.17-1.54	<0.01
	86-95	1.80	1.57-2.06	<0.01	1.86	1.62-2.14	<0.01
	95+	2.39	1.87-3.04	<0.01	2.75	2.15-3.53	<0.01
<b>gender</b>	Female	1			1		
	Male	1.21	1.10-1.33	<0.01	1.20	1.09-1.32	<0.01
<b>CCI</b>	0	1			1		
	1-2	1.54	1.35-1.77	<0.01	1.50	1.31-1.73	<0.01
	3-4	2.28	1.94-2.68	<0.01	2.10	1.78-2.48	<0.01
	5+	6.80	5.76-8.02	<0.01	7.04	5.96-8.32	<0.01
<b>SIMD</b>	Least deprived	1					
	0-20%	1.05	0.88-1.25	0.61			
	20-40%	1.12	0.94-1.33	0.21			
	40-60%	1.15	0.96-1.38	0.12			
	60-80%	1.14	0.94-1.39	0.18			

Table 3.7 to Table 3.10 shows the comparison of hazard ratio between unadjusted model and adjusted model with only one condition factor individually involved each time. Even though there were slight decrease for the hazard ratio of dementia (HR: 1.23; 95%CI: 1.05-1.44; P=0.01) and clinical delirium (HR: 1.25; 95%CI: 1.12-1.40; P<0.01), they were still significant factors for mortality (Table 3.7 and Table 3.8). However, the association between FSD and death stayed significant when the Cox's model was adjusted by FSD individually as well as gender, CCI and SIMD (HR: 1.31, 95%CI: 1.10-1.55; P<0.01) (Table 3.9). Similarly, association with CI persisted significantly in adjusted models which would increase mortality by 20% for patients with CI (Table 3.10).

*Table 3.7 Hazard ratio of all-cause mortality for dementia patients from Cox's regression model*

		Unadjusted			Adjusted		
		HR	95%CI	P-value	HR	95%CI	P-value
<b>Dementia</b>		1.42	1.22-1.66	<0.01	1.23	1.05-1.44	0.01
<b>Age group</b>	66-75	1			1		
	76-85	1.34	1.18-1.54	<0.01	1.36	1.19-1.56	<0.01
	86-95	1.80	1.57-2.06	<0.01	1.92	1.67-2.21	<0.01
	95+	2.39	1.87-3.04	<0.01	2.82	2.20-3.61	<0.01
<b>Gender</b>	Female	1			1		
	Male	1.21	1.10-1.33	<0.01	1.20	1.09-1.32	<0.01
<b>CCI</b>	0	1			1		
	1-2	1.54	1.35-1.77	<0.01	1.51	1.31-1.73	<0.01
	3-4	2.28	1.94-2.68	<0.01	2.12	1.80-2.50	<0.01
	5+	6.80	5.76-8.02	<0.01	7.08	5.99-8.38	<0.01
<b>SIMD</b>	Least deprived	1					
	0-20%	1.05	0.88-1.25	0.61			
	Most deprived						
	20-40%	1.12	0.94-1.33	0.21			
	40-60%	1.15	0.96-1.38	0.12			
	60-80%	1.14	0.94-1.39	0.18			

*Table 3.8 Hazard ratio of all-cause mortality for clinical delirium from Cox's regression model*

		Unadjusted			Adjusted		
		HR	95%CI	P-value	HR	95%CI	P-value
<b>Clinical delirium</b>		1.39	1.25-1.55	<0.01	1.25	1.12-1.40	<0.01
<b>Age group</b>	66-75	1			1		
	76-85	1.34	1.18-1.54	<0.01	1.34	1.17-1.54	<0.01
	86-95	1.80	1.57-2.06	<0.01	1.90	1.65-2.18	<0.01
	95+	2.39	1.87-3.04	<0.01	2.81	2.19-3.60	<0.01
<b>Gender</b>	Female	1			1		
	Male	1.21	1.10-1.33	<0.01	1.20	1.08-1.32	<0.01
<b>CCI</b>	0	1			1		
	1-2	1.54	1.35-1.77	<0.01	1.53	1.33-1.75	<0.01
	3-4	2.28	1.94-2.68	<0.01	2.14	1.82-2.52	<0.01
	5+	6.80	5.76-8.02	<0.01	7.07	5.98-8.36	<0.01
<b>SIMD</b>	Least deprived	1					
	0-20%	1.05	0.88-1.25	0.61			
	Most deprived						
	20-40%	1.12	0.94-1.33	0.21			
	40-60%	1.15	0.96-1.38	0.12			
	60-80%	1.14	0.94-1.39	0.18			

*Table 3.9 Hazard ratio of all-cause mortality for FSD patients from Cox's regression model*

		Unadjusted			Adjusted		
		HR	95%CI	P-value	HR	95%CI	P-value
<b>FSD</b>		1.53	1.30-1.81	<0.01	1.31	1.10-1.55	<0.01
<b>Age group</b>	66-75	1			1		
	76-85	1.34	1.18-1.54	<0.01	1.35	1.18-1.55	<0.01
	86-95	1.80	1.57-2.06	<0.01	1.91	1.67-2.20	<0.01
	95+	2.39	1.87-3.04	<0.01	2.86	2.23-3.66	<0.01
<b>Gender</b>	Female	1			1		
	Male	1.21	1.10-1.33	<0.01	1.19	1.08-1.32	<0.01
<b>CCI</b>	0	1			1		
	1-2	1.54	1.35-1.77	<0.01	1.55	1.35-1.78	<0.01
	3-4	2.28	1.94-2.68	<0.01	2.18	1.85-2.56	<0.01
	5+	6.80	5.76-8.02	<0.01	7.08	5.99-8.38	<0.01
<b>SIMD</b>	Least deprived	1					
	0-20%	1.05	0.88-1.25	0.61			
	Most deprived						
	20-40%	1.12	0.94-1.33	0.21			
	40-60%	1.15	0.96-1.38	0.12			
	60-80%	1.14	0.94-1.39	0.18			

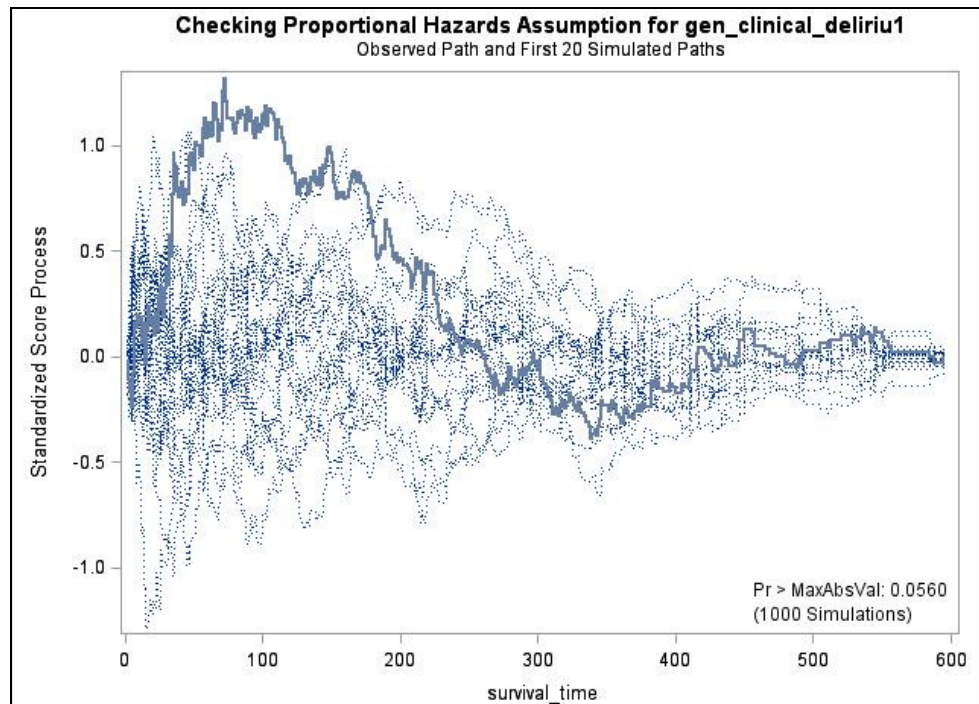
*Table 3.10 Hazard ratio of all-cause mortality for CI patients from Cox's regression model*

		Unadjusted			Adjusted		
		HR	95%CI	P-value	HR	95%CI	P-value
<b>CI</b>		1.35	1.20-1.52	<0.01	1.19	1.05-1.34	0.01
<b>Age group</b>	66-75	1			1		
	76-85	1.34	1.18-1.54	<0.01	1.35	1.18-1.55	<0.01
	86-95	1.80	1.57-2.06	<0.01	1.90	1.65-2.19	<0.01
	95+	2.39	1.87-3.04	<0.01	2.76	2.15-3.54	<0.01
<b>Gender</b>	Female	1			1		
	Male	1.21	1.10-1.33	<0.01	1.20	1.08-1.32	<0.01
<b>CCI</b>	0	1			1		
	1-2	1.54	1.35-1.77	<0.01	1.54	1.34-1.76	<0.01
	3-4	2.28	1.94-2.68	<0.01	2.17	1.84-2.55	<0.01
	5+	6.80	5.76-8.02	<0.01	7.13	6.03-8.43	<0.01
<b>SIMD</b>	Least deprived	1					
	0-20%	1.05	0.88-1.25	0.61			
	Most deprived						
	20-40%	1.12	0.94-1.33	0.21			
	40-60%	1.15	0.96-1.38	0.12			
	60-80%	1.14	0.94-1.39	0.18			

### 3.5 Checking Proportional Hazards Assumption

Figure 3.9 illustrates the results of proportional hazards assumption assessment for clinical delirium. It was found that there were apparently peak values on the graph before 300 days and the plots basically trend to be a more horizontal line after that, even though the assumption was non-significant. For a smoother curve, the patients were divided into two groups, one was clinical delirium patients survived less than 300 hundred days, and another was clinical delirium patients survived more than 300 days. Assessment of the proportional hazard ratios with these new groups can be seen from Figure 3.10 and Figure 3.11. Both time periods had non-significant results ( $P=0.64$  for less than 300 days;  $P=0.21$  for more than 300 days) which means

the validity of the proportional hazards model with these new time periods is improved. The result of Cox's regression model for clinical delirium with interacting survival time adjusted dementia, age, gender and CCI can be seen from Table 3.11. For patients who had clinical delirium, the risk of death was 4.44(95%CI: 3.93-5.03) for the first 300 days. However, if they survive more than 300 days, the risk would decrease markedly.



*Figure 3.9 Standardized Score Process for clinical delirium.*



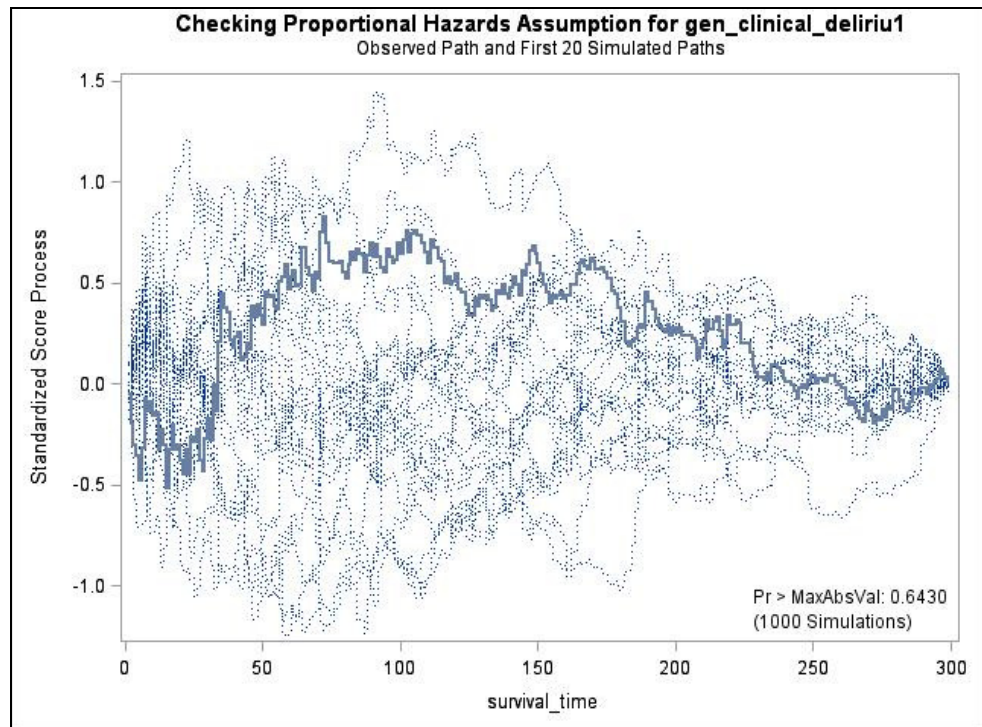


Figure 3.10 Standardized Score Process for clinical delirium with less than 300 days survive.

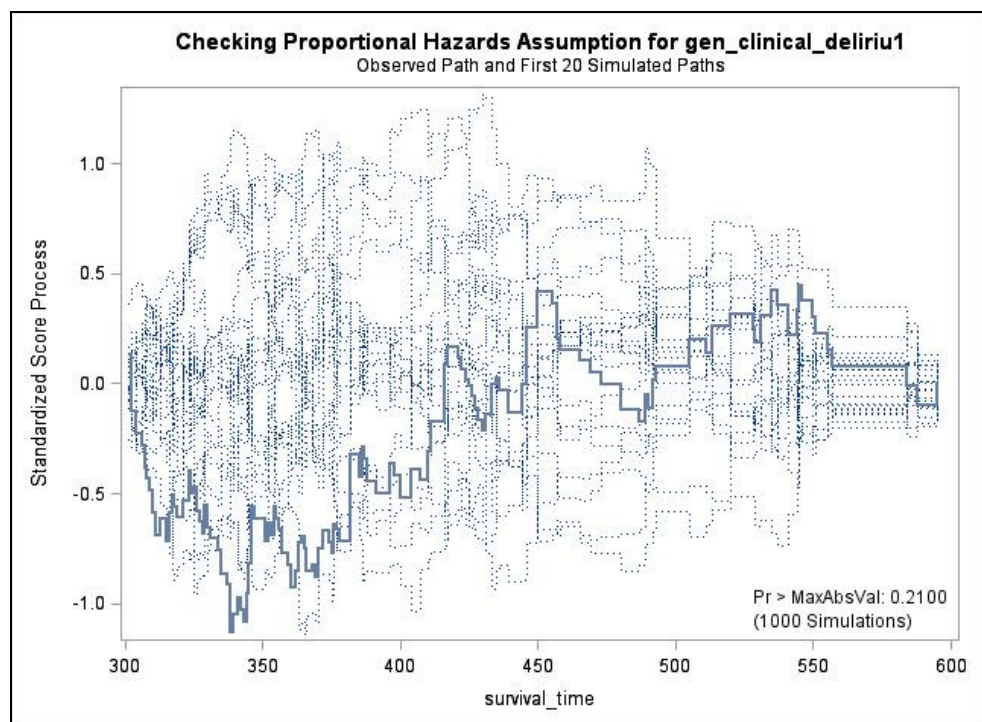


Figure 3.11 Standardized Score Process for clinical delirium with more than 300 days survive.

*Table 3.11 Hazard Ratio of all-cause mortality for clinical delirium from Cox's regression model*

		<b>HR</b>	<b>95%CI</b>	<b>P-value</b>
<b>Age group</b>	66-75	1		
	76-85	1.31	1.14-1.50	<0.01
	86-95	1.74	1.52-2.01	<0.01
	95+	2.48	1.93-3.17	<0.01
<b>CCI</b>	0	1		
	1-2	1.46	1.27-1.68	<0.01
	3-4	2	1.70-2.36	<0.01
	5+	5.67	4.79-6.72	<0.01
<b>Clinical delirium live less than 300 days</b>		4.44	3.93-5.03	<0.01
<b>Clinical delirium live more than 300 days</b>		0.2	0.15-0.26	<0.01

### 3.6 Cox's Regression Model for Mortality due to Respiratory Conditions and CVD and Survival Curves

Table 3.12 and

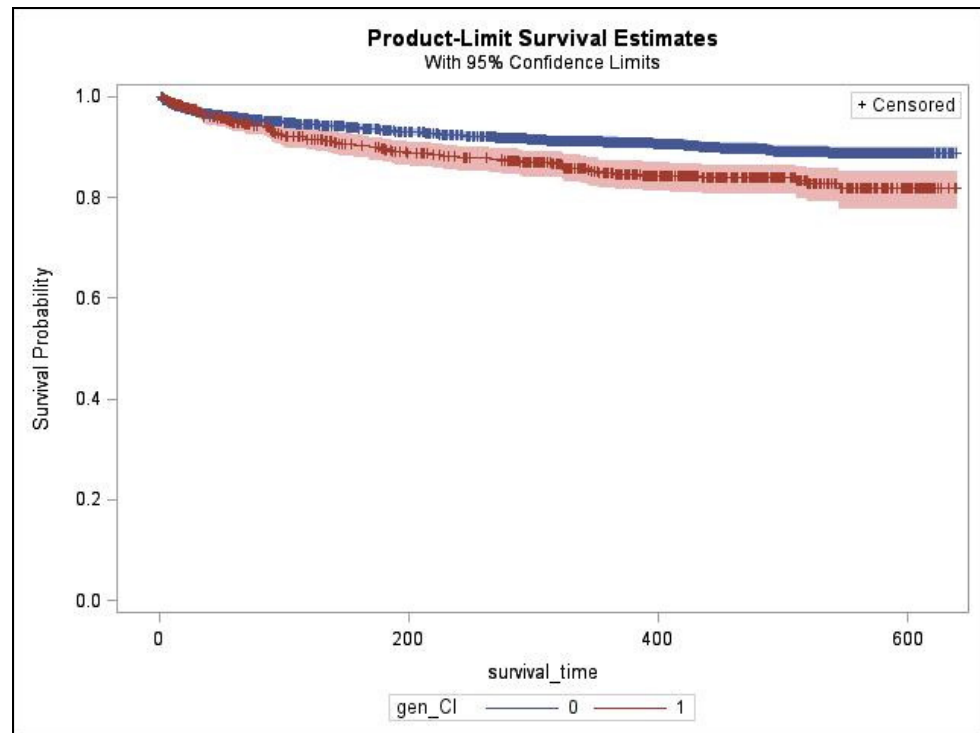
Table 3.13 show the Cox's regression models' results for the relationship between mortality due to respiratory conditions and CVD separately and adjusted for patient's cognitive condition, gender, CCI and SIMD. As a result, neither of 4 cognitive conditions was related to the death due to respiratory disease. However, male gender would significantly increase the risk of dying with respiratory disease by 68 % (HR: 1.68, 95%CI: 1.32-2.12,  $P < 0.01$ ). Only CI was estimated to having a significant relationship with co-mortality of CVD. The hazard ratio was 1.47 (95%CI: 1.20-1.79,  $P < 0.01$ ), which mean for patients with CI, the risk of dying as CVD was 47% of higher than patients without CI. Figure 3.12 was the survival curves of CVD co-mortality compared with CI and no CI. It can be easily found the difference of survival ability between them, and noCI did better in survival.

*Table 3.12 Hazard ratio of Respiratory co-mortality from Cox's regression model*

		HR	95%CI	P-value
<b>Age group</b>	66-75	1		
	76-85	1.42	1.03-1.96	0.03
	86-95	2.03	1.46-2.82	<0.01
	95+	1.98	1.00-3.90	0.05
<b>Gender</b>	Female	1		
	Male	1.68	1.32-2.12	<0.01
<b>CCI</b>	0	1		
	1-2	1.84	1.35-2.50	<0.01
	3-4	2.06	1.41-3.01	<0.01
	5+	0.55	0.22-1.39	0.21

*Table 3.13 Hazard ratio of CVD co-mortality from Cox's regression model*

		HR	95%CI	P-value
<b>CI</b>		1.47	1.20-1.79	<0.01
<b>Age group</b>	66-75	1		
	76-85	2.02	1.47-2.77	<0.01
	86-95	3.42	2.50-4.68	<0.01
	95+	5.72	3.66-8.94	<0.01
<b>CCI</b>	0	1		
	1-2	1.9	1.46-2.46	<0.01
	3-4	2.82	2.09-3.81	<0.01
	5+	1.97	1.18-3.27	0.01



*Figure 3.12 Kaplan-Meier survival Curves of CVD co-mortality for patients with and without CI (0: no CI; 1: CI)*

## 4. Discussion

### 4.1 Quality assessment tool

The assessment of risk of bias due to confounding is likely to be associated with heterogeneity between the studies. The STROBE checklist was used to assess the quality of the papers finally included. It is a common form of assessment of the quality of observational studies. It may be more suitable though for journal editors and reviewers to assess observational studies submitted to journals. In this review, the involved papers included one randomised controlled study. However, it may not be appropriate for STROBE to be used in assessing the risk of bias of the studies included. Usually, the Cochrane Collaboration tool and Newcastle-Ottawa are more appropriate in assessing quality and risk of bias for randomised trials and observational studies respectively. The latter would have been a better tool to use for this dissertation.

### 4.2 Missing data

As the dataset which was used for analysis in this dissertation was obtained directly from the statistician Professor Peter Donnan, the data had already gone through a selection process and was already clean. However, this meant that the data represented about 80% of all the potential admissions as 20% had missing data, so there is some possibility of bias in the results, although this percentage of missing would not be considered large.

### 4.3 Summary of Results

#### Outcomes of confusion

The prevalence of clinical delirium was almost 3.5 times bigger than the prevalence of FSD. It may be because there was a misdiagnosis for clinical delirium. This may provide further evidence for the poor management of delirium in clinical settings(45).

The prevalence of dementia, delirium and CI was relatively low compared with the studies included in the literature review. Maybe there was some bias during the sample selection for some of the papers which were involved in the literature review. For example, Sampson et al. (16) excluded patients who were confirmed to have delirium during the selection process. There was also a sub-sample assessment by a clinician in Whittamore's study (19). This kind of second selection process may reduce the representativeness of the results. The results from this selection method can only then represent the more focussed sample of the study. If we want to promote the results to the population, the sampling procedure should be taken into account. However, the dataset I used had linked almost all the emergency admissions in NHS Fife without selection. In addition, the assessment of confusion has become one of the routine assessments for NHS Fife emergency admission. As a result, the prevalence of dementia, delirium and CI which we got could truly represent the prevalence of all acutely admitted elderly in Fife. This may explain the consistence of prevalence of dementia of our study with Draper's (23) result. His study also came from a patient care admissions database, which avoids the bias from greater focussed selection.

As expected, the population with the four conditions were always significantly older, had shorter survival times and higher mortality than people with no conditions. Other characteristic differences between each kind of confusion patients and no confusion people existed as well, although varied each other. Dementia was more likely with female patients and dementia patients suffered more illness than people with no dementia. The latter point was consistent with results of other papers (28, 50), which found dementia was associated with many more comorbidities and more serious illness. The difference of 30 days' mortality for people with dementia and no dementia was 2.5%, but it was not significant. This result did not agree with the results of the Meta-analysis which I had done previously. It may be made worse by the significant heterogeneity of the papers in the Meta-analysis. As I mentioned before, Sampson's papers (16, 17) excluded delirium patients from the sample to concentrate on those with dementia. So the mortality was higher than other studies. Guijarro's paper was conducted for 5 years,

which may also cause the high mortality. So it may make less sense to compare the mortality related to dementia in Fife to the results of the Meta-analysis.

The overlapping between cognitive impairment, dementia and delirium were inevitable in a clinical environment. Taking consideration of this, I believed this will affect the hazard of mortality. Many factors should be considered, before conclusions can be made.

### **Survival analyses**

In the Cox model, only dementia, clinical delirium, age group, female gender and CCI were estimated to be the risk factors for death when adjusted for SIMD. The influence of FSD and CI on death was lost when adjusted for other factors. Firstly, in this study, 'general clinical delirium' and 'FSD' were both used to assess delirium. The definition of 'general clinical delirium' during the study was bound to give a higher population. This may weaken the impact of 'FSD' in adjusted analyses. Second, that mild CI was a marker of dementia has been confirmed by many studies (51, 52). CI was more often used for describing the early phase of dementia as the symptoms develop. As a result, when dementia and CI were both involved in one regression model, the influence of CI was reduced to become non-significant.

In testing for proportional hazards 300 days was found to be a key time point for clinical delirium patients during the admission in terms of mortality. As far as I know no similar result has been found. Once a patient has clinical delirium, CI may progress, be stable or reverse. Some previous studies have reported that there may be up to 50% of patients with CI who could improve their cognition status over 1 to 3 years (53, 54). These results all suggested that early detection of CI can contribute to the decrease of the mortality by early recognition and treatment of delirium.

### **Chronic disease and confusion**

Dementia, cognitive impairment and delirium have been shown to be highly prevalent with many chronic diseases, including obstructive pulmonary disease (55), vascular disease (50) and cancer (56). We focused on mortality from Respiratory disease and CVD as outcomes. As a result, only CI was found to be related to CVD when adjusted for other factors, which also suggested that CI may increase the risk of patients dying with CVD or at least may be a marker of deterioration. The

comparison between the CVD mortality in CI and no CI also demonstrated this point. This result was also consistent with the study conducted by Martin et al.(57), which suggested cognitive impairment increases the risk of cardiovascular disease and mortality.

#### 4.4 Strengths

This study is unique since I took advantage of the dataset of NHS Fife CGA programme to assess the current prevalence of confusion status and explored the relationship between all types of confusion and death. I have also linked the SMR01 dataset, GRO dataset and the CHI dataset, which guaranteed record-linkage and complete data. Besides, all the analysis was conducted under the Safe Haven within HIC , which guaranteed security and confidentiality. Investigation of all types of confusion status were assessed which is difficult as they easily overlap and generally always are underestimated during clinical settings. In my study, I not only have defined dementia, delirium and CI separately from each other, we also defined general clinical delirium and FSD to explore the diagnostic level of delirium in clinical settings. Besides, I explored all the patients admitted into hospital with a variety of diagnoses and then determined the prevalence of each kind of condition. So the outcomes of our study may be more representative than other studies.

#### 4.5 Weaknesses

There are several weaknesses in this study. First, as a cohort study, the follow-up time for the study was relatively short. Even in the best case, the maximum follow up length was only 21 months. Second, readmission rates and hospital length of stay were both vital clinical variables for estimating the influence of confusion status. However, they were not included in this study but could be in future studies. Third, before my analysis, I did not realise there was missing information for 20% of all admissions which may have introduced some bias.

The cut point of 300 days in proportional hazards ratio was the result of many attempts at data fitting. It is not an exact time point, and may differ with new datasets. More work could be done to make this cut point more accurate.



## 4.6 Implications for management of elderly patients

From my study, I found that hazard for death was related to a specific time period for identifying and controlling clinical delirium, which was 300 days. It means there will be around 10 month of time for physicians to positively diagnose and manage clinical delirium in the patients by pharmacology or other therapies. The earlier the control of clinical delirium, the lower the mortality for the patients. In addition, the result of cognitive impairment increasing the risk of cardiovascular disease and mortality should be taken seriously by all stakeholders. It should receive more attention to prevent cardiovascular disease for cognitively impaired patients during clinical care.

## 4.7 Further work

The meta-analysis could be repeated with only one of Sampson's papers instead of the two included. It was not clear that the second paper contained new results. Some results of patients within combinations of the confusion conditions could be explored further. Further analysis could be done to analyse the influence of the factors of dementia, CI and clinical delirium on the rehospitalisation rate and length of stay in hospital. Such a study should be followed up for more years to detect the long-term influence of these factors on clinical outcomes of patients. In these studies, competing risks would be an issue as death would alter the risk of rehospitalisation, for example. A clinical prediction model could also be designed to estimate risk of death within one year, which can help clinicians identify those at high risk and facilitate decisions and arrange appropriate interventions.

## 4.8 Summaries

During hospital admissions for the elderly, the four confusion conditions are prevalent worldwide. Each condition is related to worse outcomes in general hospital settings. People with dementia, delirium, cognitive impairment and FSD always do badly in terms of survival time. Dementia and delirium indeed have independent significant influence on mortality when other factors are taken into account in an adjusted Cox regression model. It is crucial to identify CI in a timely way, which

potentially could decrease mortality. For patients who have already been diagnosed with some chronic diseases, it will also benefit them if their CI can be detected early with possible treatment earlier.

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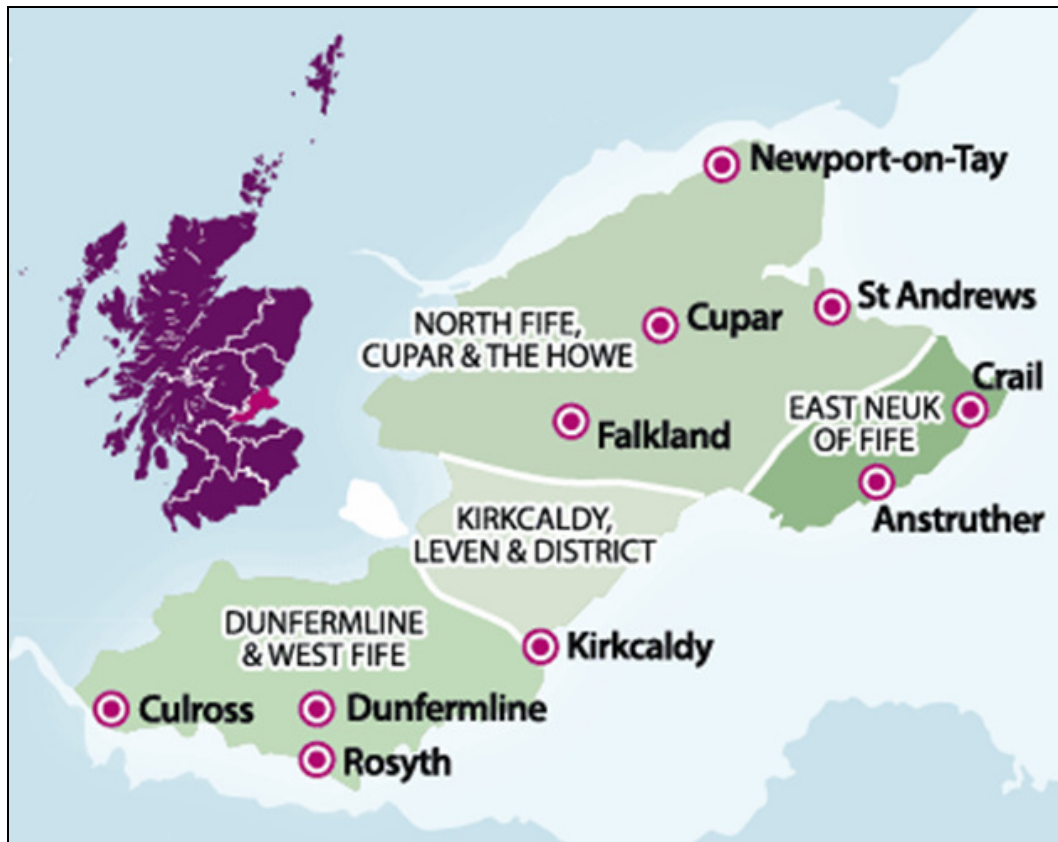
## Appendix 1 the Quality Assessment of 14 Inclusion Articles

		①a	①b	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	⑬
<b>Title and abstract</b>	Item No														
	1	A Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
		B N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Introduction</b>															
<b>Background/rationale</b>	2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Objectives</b>	3	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Methods</b>															
<b>Study design</b>	4	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y
<b>Setting</b>	5	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Participants</b>	6	A Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
		B NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<b>Variables</b>	7	Y	Y	N	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
<b>Data</b>	8	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>sources/measurement</b>															
<b>Bias</b>	9	Y	Y	Y	N	N	N	N	N	N	N	N	N	Y	N
<b>Study size</b>	10	Y	Y	N	Y	Y	Y	N	N	N	N	N	N	N	N
<b>Quantitative variables</b>	11	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	N	Y
<b>Statistical methods</b>	12	A Y	Y	N	Y	NA	Y	Y	Y	Y	N	N	N	Y	Y
		B Y	Y	N	Y	Y	N	N	N	N	N	N	N	N	Y
		C N	N	N	N	N	N	N	N	N	N	N	N	N	N
		D NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		E N	N	N	N	N	N	N	N	N	N	N	N	N	N
<b>Results</b>															
<b>Participants</b>	13	A Y	Y	N	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y
		B Y	Y	N	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y





		①a	①b	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	⑬
<b>Descriptive data</b>	14	C	Y	Y	N	N	Y	Y	N	N	N	N	N	Y	N
		A	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y
		B	N	N	N	N	N	N	N	N	N	N	N	N	N
<b>Outcome data</b>	15	C	Y	Y	NA	Y	N	Y	N	NA	N	N	NA	N	N
			Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Main results</b>	16	A	Y	Y	N	Y	N	Y	Y	Y	Y	N	N	Y	N
		B	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	Y	Y
		C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y	NA
<b>Other analyses</b>	17		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<b>Discussion</b>															
<b>Key results</b>	18		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Limitations</b>	19		Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
<b>Interpretation</b>	20		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Generalizability</b>	21		Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
<b>Other information</b>															
<b>Funding</b>	22		Y	Y	N	N	N	N	N	N	Y	Y	N	Y	N

## Appendix 2 the Region Map of Fife Scotland



# Appendix 3 Acute Comprehensive Geriatric Assessment

Social Work Services

## Acute Comprehensive Geriatric Assessment

Patient details Date and time of assessment \_\_\_\_/\_\_\_\_/\_\_\_\_ @ \_\_\_\_\_hrs

Assessed By: .....

---

**Physical Health**

Sensory impairment

Hearing  Vision

**Verbal Consent to Access Emergency Care Summary Obtained From:**

Patient

Welfare Power of Attorney/ Guardian

AWI Section 47 Certificate in Place

---

**Functional ability**

ADL score (independent (1), requires assistance (0.5), dependant (0))

Best in Previous 3 months	On admission
Washing <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Washing <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
Dressing <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Dressing <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
Going to Toilet room <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Going to toilet room <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
Transfers <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Transfers <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
Continence <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Continence <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
Eating & Drinking <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Eating & Drinking <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
Pre admission ADL score <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	Current ADL score <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>

Information from

Mobility Usual

Current

Falls Are falls cause of admission

Yes  No

Number of falls in the past year

---

**Cognitive mental health**

Dementia

Known dementia	Yes <span style="border: 1px solid black; display: inline-block; width: 20px; height: 15px; vertical-align: middle;"></span>	No <span style="border: 1px solid black; display: inline-block; width: 20px; height: 15px; vertical-align: middle;"></span>	Year of diagnosis <span style="border: 1px solid black; display: inline-block; width: 60px; height: 15px; vertical-align: middle;"></span>	Diagnosed by <span style="border: 1px solid black; display: inline-block; width: 80px; height: 15px; vertical-align: middle;"></span>	Last correspondence requested
					Yes <span style="border: 1px solid black; display: inline-block; width: 20px; height: 15px; vertical-align: middle;"></span> No <span style="border: 1px solid black; display: inline-block; width: 20px; height: 15px; vertical-align: middle;"></span> Source of Information <span style="border: 1px solid black; display: inline-block; width: 80px; height: 15px; vertical-align: middle;"></span>

Cognition Reason if AMT not completed:

---

Abbreviated Mental Test - AMT

1) What is your age? (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	5) What is the name of the hospital/residence where the patient is situated (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	9) What is the name of the present monarch? (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
2) What time is it to the nearest hour? (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	6) Can the patient recognise two persons (the doctor, nurse, home help etc)? (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	10) Count backwards from 20 to one (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>
3) Give the patient an address, ask them to repeat it at the end of the test (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	7) What is your date of birth? (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	
4) What is the year? (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	8) In what year did the first world war begin? (adjust for an event that patient would have known During childhood) (1 point) <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>	
		TOTAL SCORE <span style="border: 1px solid black; display: inline-block; width: 40px; height: 15px; vertical-align: middle;"></span>

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Delirium

Is patient drowsy? Yes ☐ No ☐ Is this a change from usual? Yes ☐ No ☐ If "YES" to both Treat as Delirium ☐

Confusion Assessment Method – CAM

Acute onset and fluctuating course

Is there evidence of an acute change in mental status from the patient's baseline? ☐

Did the (abnormal) behaviour fluctuate during the day, that is tend to come and go or increase in severity? ☐

Inattention

Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said? ☐

Disorganised thinking

Was the patient's thinking disorganised or incoherent, such as rambling or flow of ideas, or unpredictable switching from subject to subject? ☐

Score +ve ☐ -ve ☐

Clinical History Suggestive of Delirium: Yes ☐ No ☐

**Social/environmental**

Source of information AIS ☐ Contact Centre ☐ Other ☐ State:

Known to Social Work Department Yes ☐ No ☐

Package of Care

Visits per day

Coping at home ☐ ☐

Details of Social Work Input or specific care provided.

If no details of problems

Social history/living situation

Lives alone ☐ Care Home ☐ Lives with spouse ☐ Hospital ☐ With family ☐ Sheltered ☐

**Collateral History**

Information from

Current living situation highlight issues

Change in functional ability

Change in cognition mood disturbance

Other e.g. legal (POA – Name)  Copy of POA requested Yes / No /NA

**Outcome**

Care of the Elderly ☐ Other ☐

**S/C/N Review (MoE)**

Care of the Elderly ☐ Other ☐

**Management /Identified Pathways**

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## Appendix 4the Local SIMD Summary for Fife

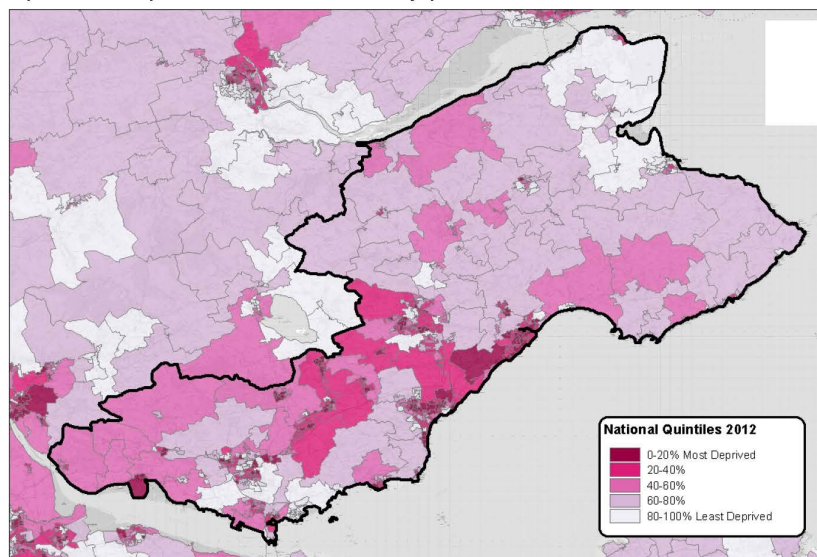
### Local Authority Summary – SIMD 2012

#### Fife

<http://simd.scotland.gov.uk/publication-2012>

This provides a summary of key findings from the Scottish Index of Multiple Deprivation (SIMD 2012) published on 18 December 2012.

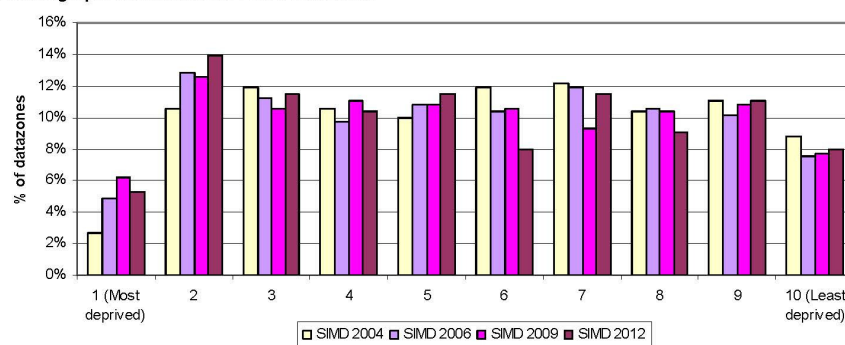
Map: Levels of deprivation in Fife in SIMD 2012 by quintile



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The decile graph shows what percentage of Fife's datazones are found in each of the SIMD deciles. Fife's datazones are distributed relatively evenly across the less deprived, middle, and more deprived deciles in SIMD 2012. This is similar to the pattern observed for SIMD 2009.

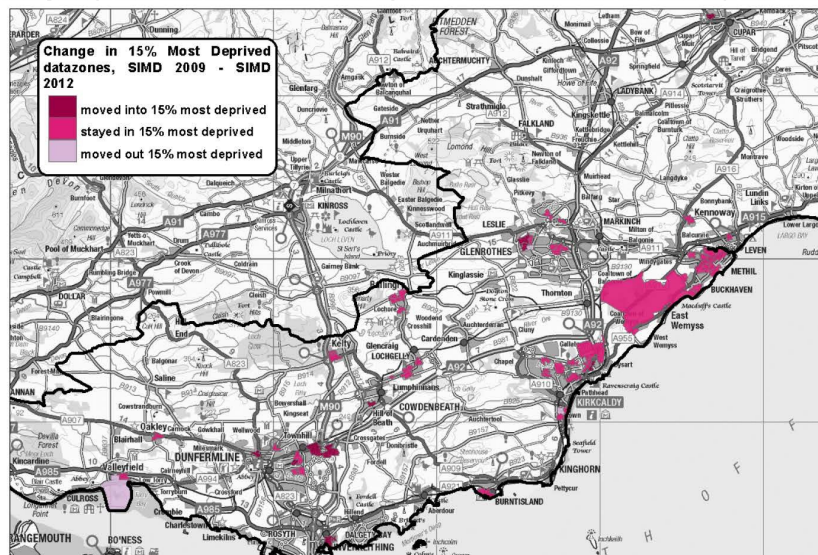
Decile graph: distribution of Fife's datazones



### Most deprived datazone in Fife

The most deprived datazone in Fife in the overall SIMD 2012 is S01002779, which is found in the Intermediate Zone of Kirkcaldy Gallatown and Sinclairtown and the Scottish Parliament Constituency of Kirkcaldy. It has a rank of 82, meaning that it is amongst the 5% most deprived areas in Scotland.

### Change map: datazones in Fife which have stayed in or moved out of the 15% most deprived in Scotland



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The map shows the areas within Fife which have moved into the 15% most deprived, stayed in the 15% most deprived or moved out the 15% most deprived areas between SIMD 2009 and SIMD 2012.

### National Share of most deprived areas

In SIMD 2012, 58 (5.9%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 51 (5.2%) in 2009, 47 (4.8%) in 2006 and 34 (3.5%) in 2004. The 2012 share is displayed in the barcode chart.

The barcode chart shows the position of the local authority's datazones in the Scotland-wide ranking. Each bar on the barcode represents a datazone in the local authority and is positioned according to its deprivation rank: the more deprived a datazone is, the further to the left it will be positioned.

### Barcode chart: distribution of Fife's datazones in SIMD 2012



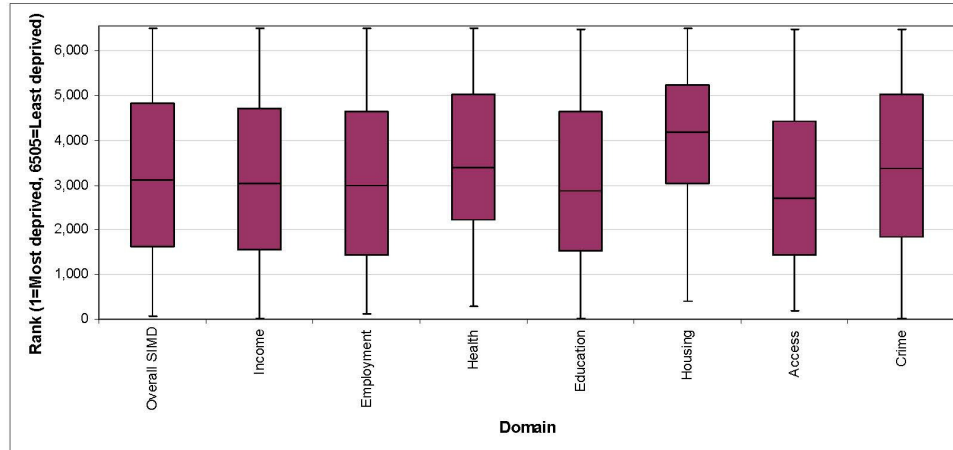
### Local Share of most deprived areas

In SIMD 2012, 58 (12.8%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 51 (11.3%) in 2009, 47 (10.4%) in 2006 and 34 (7.5%) in 2004.

### Individual domains

The box plot summarises the range of values for the overall SIMD and the seven domains which make up the SIMD. In the following sections the individual domains are examined in more detail.

**Box plot: Fife's ranks in the overall SIMD 2012 and individual SIMD domains. Boxes show the middle 50% of values and the middle (median) value; whiskers show the minimum and maximum ranks.**



### Income Domain

The level of income deprivation in Fife is below that in Scotland as a whole. In the SIMD 2012 income domain, 13.3% of the population of Fife were income deprived. This compares to 13.4% across Scotland as a whole.

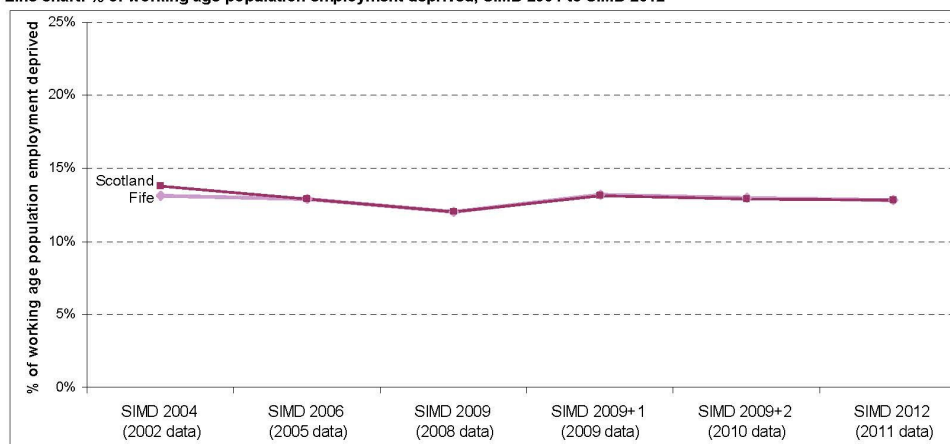
- *National share:* On the income domain in SIMD 2012, 65 (6.7%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 51 (5.2%) in 2009, 49 (5%) in 2006 and 43 (4.4%) in 2004.
- *Local share:* On the income domain in SIMD 2012, 65 (14.3%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 51 (11.3%) in 2009, 49 (10.8%) in 2006 and 43 (9.5%) in 2004.
- The most income deprived datazone in Fife in SIMD 2012 is S01002779, which is found in the Intermediate Zone of Kirkcaldy Gallatown and Sinclairtown and the Scottish Parliament Constituency of Kirkcaldy. It has a rank of 25, meaning that it is amongst the 5% most income deprived areas in Scotland.



## Employment Domain

The level of employment deprivation in Fife is below that in Scotland as a whole. In the SIMD 2012 employment domain, 12.8% of the population of Fife aged 16-60/64 were employment deprived. This compares to 12.8% across Scotland as a whole (see line chart).

Line chart: % of working age population employment deprived, SIMD 2004 to SIMD 2012



- **National share:** In the employment domain in SIMD 2012, 65 (6.7%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 67 (6.9%) in 2009, 67 (6.9%) in 2006 and 49 (5%) in 2004.
- **Local share:** In the employment domain in SIMD 2012, 65 (14.3%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 67 (14.8%) in 2009, 67 (14.8%) in 2006 and 49 (10.8%) in 2004.
- The most employment deprived datazone in Fife in SIMD 2012 is S01002655, which is found in the Intermediate Zone of Dunfermline Abbeyview North and the Scottish Parliament Constituency of Dunfermline West. It has a rank of 128, meaning that it is amongst the 5% most employment deprived areas in Scotland.

## Health Domain

- **National share:** In the health domain in SIMD 2012, 15 (1.5%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 17 (1.7%) in 2009, 14 (1.4%) in 2006 and 15 (1.5%) in 2004.
- **Local share:** In the health domain in SIMD 2012, 15 (3.3%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 17 (3.8%) in 2009, 14 (3.1%) in 2006 and 15 (3.3%) in 2004.
- The most health deprived datazone in Fife in SIMD 2012 is S01002856, which is found in the Intermediate Zone of Methil East and the Scottish Parliament Constituency of Central Fife. It has a rank of 285, meaning that it is amongst the 5% most health deprived areas in Scotland.

## Education Domain

- **National share:** In the education domain in SIMD 2012, 68 (7%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 65 (6.7%) in 2009, 49 (5%) in 2006 and 48 (4.9%) in 2004.
- **Local share:** In the education domain in SIMD 2012, 68 (15%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 65 (14.3%) in 2009, 49 (10.8%) in 2006 and 48 (10.6%) in 2004.



- The most education deprived datazone in Fife in SIMD 2012 is S01002775, which is found in the Intermediate Zone of Kirkcaldy Hayfield and Smeaton and the Scottish Parliament Constituency of Kirkcaldy. It has a rank of 27, meaning that it is amongst the 5% most education deprived areas in Scotland.

#### **Housing Domain**

- *National share:* On the housing domain in SIMD 2012, 5 (0.5%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife.
- *Local share:* On the housing domain in SIMD 2012, 5 (1.1%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland.
- The most housing deprived datazone in Fife in SIMD 2012 is S01002995, which is found in the Intermediate Zone of St Andrews Central and the Scottish Parliament Constituency of North East Fife. It has a rank of 416, meaning that it is amongst the 10% most housing deprived areas in Scotland.

#### **Access Domain**

- *National share:* In the access domain in SIMD 2012, 60 (6.1%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 54 (5.5%) in 2009, 67 (6.9%) in 2006 and 43 (4.4%) in 2004.
- *Local share:* In the access domain in SIMD 2012, 60 (13.2%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 54 (11.9%) in 2009, 67 (14.8%) in 2006 and 43 (9.5%) in 2004.
- The most access deprived datazone in Fife in SIMD 2012 is S01003003, which is found in the Intermediate Zone of Newburgh and the Scottish Parliament Constituency of North East Fife. It has a rank of 197, meaning that it is amongst the 5% most access deprived areas in Scotland.

#### **Crime Domain**

- *National share:* In the crime domain in SIMD 2012, 54 (5.5%) of the 976 datazones in the 15% most deprived datazones in Scotland were found in Fife, compared to 69 (7.1%) in 2009 and 93 (9.5%) in 2006.
- *Local share:* In the crime domain in SIMD 2012, 54 (11.9%) of Fife's 453 datazones were found in the 15% most deprived datazones in Scotland, compared to 69 (15.2%) in 2009 and 93 (20.5%) in 2006.
- The most crime deprived datazone in Fife in SIMD 2012 is S01002722, which is found in the Intermediate Zone of Kirkcaldy Central and the Scottish Parliament Constituency of Kirkcaldy. It has a rank of 30, meaning that it is amongst the 5% most crime deprived areas in Scotland.

## Appendix 5 SAS Syntax for Data Analysis

```

libname alldata 'Z:\test';
libname xportout xport 'Z:\test\CGA_all_admissions.xpt';
data alldata.xportout;
set xportout.cga_all_;
run;
data alldata.partly;
set alldata.xportout (keep= prochi sex age ADMISSIO
DISCHARG SIMD_SCT SIMD_SC2 DEMENTI2);
run;
/*in this process I first set a new excel documents which
contain the variables I want, and then import it*/
data ALLDATA.useful ;
infile 'Z:\test\CGA_useful.csv' delimiter =
', ' MISOVERDSDlrecl=32767 firstobs=2 ;
informat prochi $10. ;
informat sex $1. ;
informat age best32. ;
informat admission_date_detail ddmmyy10. ;
informat discharge_date_detail ddmmyy10. ;
informat simd_sct_quintile best32. ;
informat simd_sct_decile best32. ;
informat dementia best32. ;
informat gen_clinical_delirium best32. ;
informat gen_FSD best32. ;
informat gen_CI best32. ;
informat CCI best32. ;
format prochi $10. ;
format sex $1. ;
format age best12. ;
format admission_date_detail ddmmyy10. ;
format discharge_date_detail ddmmyy10. ;
format simd_sct_quintile best12. ;
format simd_sct_decile best12. ;
format dementia best12. ;
format gen_clinical_delirium best12. ;
format gen_FSD best12. ;
format gen_CI best12. ;
format CCI best12. ;
input
prochi $
sex $
age
admission_date_detail
discharge_date_detail
simd_sct_quintile
simd_sct_decile
dementia
gen_clinical_delirium
gen_FSD
gen_CI
CCI;

run;
/*import the death and ICD data*/

data ALLDATA.USEFUL2 ;

```

```

infile 'P:\Project 2702- NHS Fife Comprehensive Geriatric
Assessment\jzang2702\CGA
Jinnan\Project_2702_GRO_CGA_Cohort.csv' delimiter
', 'MISSOVERDSDlrecl=32767firstobs=2;
informat PROCHI $10. ;
informat date_of_death_GROddmmyy10. ;
informat icdcucd $4. ;
informat icdrcd0 $4. ;
informat icdrcd1 $4. ;
informat icdrcd2 $4. ;
informat icdrcd3 $4. ;
informat icdrcd4 $4. ;
informat icdrcd5 $4. ;
informat icdrcd6 $4. ;
informat icdrcd7 $4. ;
informat icdrcd8 $4. ;
informat icdrcd9 $4. ;
informat hb_codebest32. ;
informat dt_regddmmyy10. ;
informat inst_code $5. ;
format PROCHI $10. ;
format date_of_death_GROddmmyy10. ;
format icdcucd $4. ;
format icdrcd0 $4. ;
format icdrcd1 $4. ;
format icdrcd2 $4. ;
format icdrcd3 $4. ;
format icdrcd4 $4. ;
format icdrcd5 $4. ;
format icdrcd6 $4. ;
format icdrcd7 $4. ;
format icdrcd8 $4. ;
format icdrcd9 $4. ;
format hb_codebest12. ;
format dt_regddmmyy10. ;
format inst_code $5. ;
input
PROCHI $
date_of_death_GRO
icdcucd $
icdrcd0 $
icdrcd1 $
icdrcd2 $
icdrcd3 $
icdrcd4 $
icdrcd5 $
icdrcd6 $
icdrcd7 $
icdrcd8 $
icdrcd9 $
hb_code
dt_reg
inst_code $;
run;
/*keep the variable I want from dataset*/
data alldata.useful2;
set alldata.useful2 (keep=PROCHI date_of_death_GROicdcucd
icdrcd0);
run;
proc sort data=alldata.useful2 ;

```

```

by PROCHI;
run;
/*as the data in useful2 include a record with missing*/
data alldata.useful2;
set alldata.useful2;
if date_of_death_GRO="." then delete;
run;
proc sort data=alldata.useful ;
by PROCHI;
run;
/*merge two dataset together, but useful2 may have people
who are not followed up, we need delete them*/
data alldata.whole;
merge alldata.useful(in=a) alldata.useful2(in=b);
by PROCHI ;
if not a then delete;
run;
/*set a new variable to show if the patient has been dead*/
data alldata.whole1;
set alldata.whole;
if date_of_death_GRO=" " then death=0;
else death=1;
run;
/*if patient have two record, we just keep the first
record*/
data alldata.whole1;
set alldata.whole1;
by PROCHI;
first=first.PROCHI;
last=last.PROCHI;
run;
/*KEEP THE FIRST VISIT RECORD*/
data try;
set alldata.whole1;
by PROCHI;
if first.PROCHI then cnt=0;
cnt+1;
if cnt<=1;
run;
data single dup;
set alldata.whole1;
by PROCHI;
if first.PROCHI and last.PROCHI then output single;
else output dup;
run;

/*set 4*4 tables with dementia, gen_clinical_delirium
, gen_FSD, gen_CI, CCI, death*/
proc freq data=try ;
tables sex*dementia / chisq;
title gender and dementia;
run;
proc freq data=try ;
tables sex*gen_clinical_delirium / chisq;
title gender and clinical delirium;
run;
proc freq data=try ;
tables sex*gen_FSD / chisq;
title gender and fully syndromic delirium;
run;
proc freq data=try;

```

```

tables sex*gen_CI/ chisq;
title gender and cognitive impairment;
run;
proc freq data=try;
tables sex*death/ chisq;
title gender and death;
run;
proc freq data=try;
tables sex*CCI/ chisq;
title gender and charlson comorbidity index;
run;
/*to find the start date and end date of the record,start
date(01/01/2012) end date(30/09/2013)*/
proc sort data=work.try;
by date_of_death_GRO;
run;
/*if the patient still alive until the end,modify their
missing data into the end date(30/09/2013)*/
data try;
set try;
if date_of_death_GRO=. then date_of_death_GRO="30SEP2013"D;
run;
/*delete the false record*/
data try;
set try;
if date_of_death_GRO<"01JAN2012"D then delete;
run;
/*set a new variable named survival_time,look out there
should be a +1, in case of the patient dead same day*/
data try;
set try;
survival_time=date_of_death_GRO-admission_date_detail+1;
run;
proc sort data=work.try;
by PROCHI;
run;
/*plot Kaplan-Meier estimator and its 95% confidence
interval, with people with and without dementia, also have a log-
test*/

odshtmlgpath='z:\\survival graphs';
ods graphics on / outputfmt =jpeg;
proc lifetest data=try plots=(survival (cl));
timesurvival_time*death(0);
strata dementia / test= (all);
title Kaplan-Meier estimator of dementia;
run;

proc lifetest data=try plots=(survival (cl));
timesurvival_time*death(0);
strata gen_clinical_delirium/ test= (all);
title Kaplan-Meier estimator of gen_clinical_delirium;
run;
proc lifetest data=try plots=(survival (cl));
timesurvival_time*death(0);
strata gen_FSD/ test= (all);
title Kaplan-Meier estimator of gen_FSD;
run;
proc lifetest data=try plots=(survival (cl));
timesurvival_time*death(0);
strata gen_CI/ test= (all);

```

```

title Kaplan-Meier estimator of gen_CI;
run;
/*to compare between age, seperate age into 4 group*/
data try;
set try;
if 65< age <=75 then age_group=1;
elseif 75< age <=85 then age_group=2;
elseif 85< age <=95 then age_group=3;
elseif 95< age then age_group=4;
run;
data try;
set try;
if CCI=0 then CCI_cat=1;
elseif 1<= CCI <=2 then CCI_cat=2;
elseif 3<= CCI <=4 then CCI_cat=3;
elseif 5<= CCI then CCI_cat=4;
run;
proc lifetest data=try plots=(survival (cl));
time survival_time*death(0);
strata age_group / test= (all);
title Kaplan-Meier estimator of age_group;
run;
proc lifetest data=try plots=(survival (cl));
time survival_time*death(0);
strata CCI_cat / test= (all);
title Kaplan-Meier estimator of charlson comorbidity index;
run;
proc lifetest data=try plots=(survival (cl));
time survival_time*death(0);
strata sex / test= (all);
title Kaplan-Meier estimator of sex;
run;
proc lifetest data=try plots=(survival (cl));
time survival_time*death(0);
strata simd_sct_quintile / test= (all);
title Kaplan-Meier estimator of SIMD;
run;
proc freq data=try ;
tables dementia*gen_clinical_delirium*gen_CI / chisq;
title mix three table;
run;
/*To do the characteristics analyse with the
ANOVA(univariate) and chi square(chisq) test*/
data try;
set try;
proc univariate data=try ;
class dementia;
var CCI;
run;
proc freq data=try ;
tables CCI_cat*dementia / chisq;
run;
/*Cox's regression model, with the first value as the
reference*/
proc phreg data=try ;
class dementia gen_clinical_delirium gen_FSD gen_CI age_group
sex CCI_cat simd_sct_quintile / ref=first ;
model survival_time*death(0)= dementia
gen_clinical_delirium gen_FSD gen_CI
age_group sex CCI_cat simd_sct_quintile / rlselection=b;
run;

```

```

/*Cox's proportional hazard ratio test (with "assess"
statement)*/
odshtmlgpath='z:\\PH HR';
odsgraphicson / outputfmt =jpeg;
procphregdata=try ;
class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
model survival_time*death(0)= dementia
gen_clinical_deliriumgen_FSDgen_CI
age_group sex CCI_catsimd_sct_quintile/rlselection=b;
assessph/ resample;
run;
/*use spearman relation test to fit the relationship
between CI and dementia/clinical delirium/FSD */
proccorrdata=try spearman;
var dementia gen_CI;
run;
proccorrdata=try spearman;
var gen_clinical_deliriumgen_CI;
run;
proccorrdata=try spearman;
var gen_FSDgen_CI;
run;
proccorrdata=try spearman;
var gen_FSDgen_clinical_delirium;
run;
proccorrdata=try spearman;
var gen_FSD dementia;
run;
proccorrdata=try spearman;
var gen_clinical_delirium dementia;
run;
/*fit the cox's model with just one condition itself*/
procphregdata=try ;
class dementia age_group sex CCI_catsimd_sct_quintile
/ref=first ;
model survival_time*death(0)= dementia
age_group sex CCI_catsimd_sct_quintile/rl ;
run;
procphregdata=try ;
class gen_clinical_deliriumage_group sex
CCI_catsimd_sct_quintile /ref=first ;
model survival_time*death(0)= gen_clinical_delirium
age_group sex CCI_catsimd_sct_quintile/rl ;
run;
procphregdata=try ;
class gen_FSDage_group sex CCI_catsimd_sct_quintile
/ref=first ;
model survival_time*death(0)= gen_FSD
age_group sex CCI_catsimd_sct_quintile/rl ;
run;
procphregdata=try ;
class gen_CIage_group sex CCI_catsimd_sct_quintile
/ref=first ;
model survival_time*death(0)= gen_CI
age_group sex CCI_catsimd_sct_quintile/rl ;
run;
/*fit the cox's model with each factor*/
procphregdata=try ;
class simd_sct_quintile /ref=last ;
model survival_time*death(0)= simd_sct_quintile/rl ;

```

```

/*extracted RESP and CVD from ICD, do Kaplan-Meier plots for
co-mortality of CVD*/
data ICD;
set try; by PROCHI;
ICD= put (icdcucd,4.-L);
adm=substr(ICD,1,1);
formatadm$4.;
run;
data ICD;
set ICD;
ifadm= "J"thendeath_reason= "RESP";
elseifadm= "I"thendeath_reason= "CVD";
elseifadm= " "thendeath_reason= " ";
elsedeath_reason= "OTHERS";
run;
data ICD;
set ICD;
ifdeath_reason= "RESP"then RESP= 1;
else RESP= 0;
run;
data ICD;
set ICD;
ifdeath_reason= "CVD"then CVD= 1;
else CVD= 0;
run;
odshtmlgpath='z:\\survival graphs';
odsgraphicson / outputfmt =jpeg;
proclifetestdata=icdplots=(survival (cl));
timesurvival_time*CVD(0);
stratagen_CI / test= (all);
title Kaplan-Meier estimator of co-mortality of CVD;
run;

/*Cox's regression model with the icd dataset to test the
relationship between co-mortality of RESP and other factorS,
with the first value as the refernce*/
procphregdata=icd ;
class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
modelsurvival_time*RESP(0)= dementia
gen_clinical_deliriumgen_FSDgen_CI
age_group sex CCI_catsimd_sct_quintile /rlselection=b;
run;
/*Cox's proportional hazard ratio test (with "assess"
statement)*/
odshtmlgpath='z:\\PH HR';
odsgraphicson / outputfmt =jpeg;
procphregdata=icd ;
class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
modelsurvival_time*RESP(0)= dementia
gen_clinical_deliriumgen_FSDgen_CI
age_group sex CCI_catsimd_sct_quintile /rlselection=b;
assessph/ resample;
run;
/*Cox's regression model with the icd dataset to test the
relationship between co-mortality of CVD and other factorS,
with the first value as the refernce*/
procphregdata=icd ;
class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;

```



```

        model survival_time*CVD(0)=                                dementia
gen_clinical_deliriumgen_FSDgen_CI
    age_group sex CCI_catsimd_sct_quintile /rlselection=b;
    run;
    /*Cox's proportional hazard ratio test    (with "assess"
statement)*/
    odshtmlgpath='z:\\PH HR';
    odsgraphicson / outputfmt =jpeg;
    procphregdata=icd ;
    class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
    model survival_time*CVD(0)=                                dementia
gen_clinical_deliriumgen_FSDgen_CI
    age_group sex CCI_catsimd_sct_quintile /rlselection=b;
    assessph/ resample;
    run;
    procphregdata=try ;
    class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
    model survival_time*death(0)=                                dementia
gen_clinical_deliriumgen_FSDgen_CI
    age_group sex CCI_catsimd_sct_quintile/rlselection=b;
    run;
    data less;
    set try;
    by PROCHI;
    if survival_time>300thendelete;
    run;
    procphregdata=less ;
    class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
    model survival_time*death(0)=                                dementia
gen_clinical_deliriumgen_FSDgen_CI
    age_group sex CCI_catsimd_sct_quintile/rl ;
    run;
    odshtmlgpath='z:\\PH HR';
    odsgraphicson / outputfmt =jpeg;
    procphregdata=less ;
    class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
    model survival_time*death(0)=                                dementia
gen_clinical_deliriumgen_FSDgen_CI
    age_group sex CCI_catsimd_sct_quintile/rl ;
    assessph/ resample;
    run;
    data more;
    set try;
    by PROCHI;
    if survival_time<= 300thendelete;
    run;

    procphregdata=more ;
    class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
    model survival_time*death(0)=                                dementia
gen_clinical_deliriumgen_FSDgen_CI
    age_group sex CCI_catsimd_sct_quintile/rl ;
    run;
    odshtmlgpath='z:\\PH HR';
    odsgraphicson / outputfmt =jpeg;
    procphregdata=more ;

```

```

class dementia gen_clinical_deliriumgen_FSDgen_CIage_group
sex CCI_catsimd_sct_quintile /ref=first ;
model survival_time*death(0)= dementia
gen_clinical_deliriumgen_FSDgen_CI
age_group sex CCI_catsimd_sct_quintile/r1 ;
assessph/ resample;
run;
/*set up a new variable 'time_split', use 300 days. AS WE
FOUND THAT BEFORE 300 DAYS, THE PROPORTIONAL HAZRD RATIO WAS NOT
A
STABLE LINE*/
data split;
set try;
by PROCHI;
if survival_time<= 300 then time_split=0;
else time_split=1;
run;
/*SET UP TWO NEW VARIABLES 'GCD_GT_300' AND
'GCD_LT_300', 'GCD_GT_300' WAS PEOPLE WITH GCD AND SURVIVAL MORE
THAN 300DAYS
'GCD_LT_300' WAS PEOPLE WITH GCD AND SURVIVAL LESS THAN 300
DAYS.*/
data splitnew;
set split;
by PROCHI;
gcd_gt_300=gen_clinical_delirium*time_split;
gcd_lt_300=gen_clinical_delirium*(1-time_split);
run;

/* DO THE COX MODEL WITH 'GCD_GT_300' AND 'GCD_LT_300'*/
proc phreg data=splitnew ;
class dementia age_group sex CCI_cat /ref=first ;
model survival_time*death(0)= dementia
age_group sex CCI_cat gcd_gt_300 gcd_lt_300 /r1 ;
run;
/*to check 30 days/ 6 month/ 12 month mortality of
dementia, delirium and cognitive impairment*/
data mortality;
set try;
if survival_time<=30 then death_30days=1;
else death_30days=0;
run;
data mortality;
set try;
if survival_time<=180 then death_180days=1;
else death_180days=0;
run;
data mortality;
set try;
if survival_time<=360 then death_360days=1;
else death_360days=0;
run;
proc freq data=mortality ;
tables death_180days* gen_CI / chisq;
run;

```